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EXPERIMENTAL STUDIES ON HEADACHE

TRANSIENT THICKENING OF WALLS OF CRANIAL ARTERIES IN RELATION TO CERTAIN PHENOMENA OF MIGRAINE HEADACHE AND ACTION OF ERGOTAMINE TARTRATE ON THICKENED VESSELS

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Distention of cranial arteries induces pain of an aching quality.[1] On the other hand, when the distended cranial arteries associated with the attack of migraine headache are constricted, the pain is abolished.[2] The speed with which vasoconstrictor agents, such as ergotamine tartrate, reduce the intensity of the headache approximates the rate of constriction of the cranial arteries. In many patients the headache arises in the distended branches of the external carotid arteries,[3] although any or all of the cranial arteries may be involved at one time or another in migraine headache. Secondary to such pain from prolonged distention of cranial arteries, the skeletal muscles of the neck and scalp contract. Such prolonged contraction in itself becomes painful and adds a component to the migraine headache.[4]

Certain additional phenomena of the migraine headache which have not been studied before are the subject of this discussion. They may be described as follows: After several hours of migraine headache, involving for example the temporal artery, the vessel may appear more prominent and distended than normal and becomes more readily palpable through the skin. Further, instead of being readily collapsible, it becomes rigid, pipelike and less readily compressible by the palpating finger. Also, the artery may be tender when compressed. Patients so affected may report that after the first hour or two of an attack of migraine headache the quality of the headache changed in that the initial pulsating or throbbing was less conspicuous or was absent and the pain became a steady ache.

To account for these changes, we have postulated that after sustained dilatation there occurs a transient change in the structure of the wall of the temporal artery, namely, thickening or edema of the muscular and adventitial structures. To validate this conception, sections taken from the temporal artery of patients during attacks of migraine headache involving this structure were studied. Microscopic examination of such sections suggested that there was thickening of the arterial wall. However, exactly comparable control sections of the same or other arteries during periods of freedom from headache cannot be obtained.

It has been necessary, therefore, to approach the problem through animal studies by determining whether transient changes within the arterial walls, such as are relevant to this discussion, can follow prolonged vasodilatation.

To achieve this end, the use of a vasodilator agent, preferably one present in the body, was desirable. Acetylcholine was selected. It is emphasized that the selection was not based on evidence that acetylcholine causes migraine headache; the drug was chosen because it is an active vasodilator, is promptly destroyed locally and can be infused for several hours without endangering the

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From the New York Hospital and the Departments of Medicine (Neurology) and Psychiatry, Cornell University Medical College.

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2. Graham, J. R., and Wolff, H. G.: Mechanism of Migraine Headache and Action of Ergotamine Tartrate, A. Research Nerv. & Ment. Dis., Proc. **18**:638, 1938; Arch. Neurol. & Psychiat. **39**:737 (April) 1938. Sutherland, A. M., and Wolff, H. G.: Experimental Studies on Headache: Further Analysis of the Mechanism of Headache in Migraine, Hypertension and Fever, ibid. **44**:929 (Nov.) 1940.

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life of the animal. It is suggested that the thickening of arterial walls demonstrated in the following experiments may be analogous to transient thickening of arterials walls during a prolonged attack of migraine headache.

EXPERIMENTS WITH A VASODILATOR SUBSTANCE

Method.—Six cats were anesthetized with an aqueous solution of dial with ethyl carbamate and monoethylurea. One ear was removed as a control for histologic study. Mammalian Ringer's solution[5] containing 0.5 mg. of acetylcholine bromide per hundred cubic centimeters was infused into the common carotid artery on the side of the intact ear by inserting a hypodermic needle into a branch with the tip of the needle reaching the common carotid artery and pointing in the direction of the blood stream. The rate of inflow (ascertained by a drop recorder in the inflow circuit) was so adjusted that the total input of the acetylcholine solution during the two hours of infusion was 10 cc.

The blood pressure was registered by means of a cannula inserted into the femoral artery and leading to a mercury manometer. Acetylcholine in the concentrations used induced no significant changes in the blood pressure, the heart rate or the rate of respiration.

After two hours of infusion the remaining ear was removed. The ears were fixed in Bouin's solution, and cross sections were prepared for histologic study. Five strips of tissue were cut from each ear, the corresponding strips being equidistant from the tip. The strips were approximately 2 mm. wide, and the sites from which they were taken were separated from each other by about 2 mm. The strips were, therefore, representative samples of the ear from tip to base. Each strip was divided into two to four pieces for convenience in cutting and mounting. From one to three sections for histologic study were made from each piece, making twelve to twenty sections from each ear. The sections were prepared with the trichrome stain.[6] The width of the walls of all arteries containing visible smooth muscle was measured. An area of the cross section of the wall, including intima, stratum muscularis and adventitia, of each of the arteries was projected onto paper by means of a camera lucida, using a magnification of 15 by 40, and a tracing made. This area was then measured with a planimeter. From 100 to 250 cross sections of arteries from each ear were thus measured.

Frozen sections were also prepared. These sections showed changes similar to those noted in ears fixed with Bouin's solution; but since the frozen sections were technically less satisfactory for measuring, the results have not been included in the data presented.

Results.—On gross inspection the infused ears were noted to be slightly thicker than the control ears; and when they were compressed between the fingers, pitting was observed. The infused ears were redder, and the blood vessels appeared larger. Irregularly scattered about were small, reddened regions, presumably the result of diapedesis.

Microscopic examination showed that the walls of the arteries of the infused ears were sometimes thickened. Here and there the intima was slightly swollen, and the nuclei of the smooth muscle cells were farther apart than normal. There was no cellular exudate or hyperplasia. It seemed, then, not only that the arteries were dilated but that their walls were thicker.

Cross Sectional Areas of the Walls of Arteries of Ears Infused with a Vasodilator Substance (Acetylcholine) and of Control Ears *

	Cross Section Area of Wall				
	0.5 to 0.75 Sq. Cm.		5 to 7. 5 Sq. Cm.		0.5 to 7.5 Sq. Cm.
Procedure	Number of Arteries, %	Total Area of the Cross Sections Within the Group, Sq. Cm.	Number of Arteries, %	Total Area of the Cross Sections Within the Group, Sq. Cm.	Total Area of Cross Sections of the Walls per 100 Arteries, Sq. Cm.
Control	21.0	12.80	3.6	19.40	185.50
Ear infused with acetylcholine	12.0	7.50	18.3	109.00	268.00

* The values given are the values for the projected (camera lucida) sections and not actual dimensions of arteries.

Measurements of the projected areas of cross sections of the arterial walls are summarized in the table. These quantitative data are expressions of the magnifications of the camera lucida and the microscope and do not represent actual dimensions of the arteries. The arteries were classified according to magnitude of the projected areas of the cross sections into eleven groups. The magnified thickness of the walls varied from 5 to 48 mm. Sections from the control series had a larger number of arteries with the smallest cross section area of the wall, whereas the infused ears had a larger number of arteries with the greatest cross section area of the wall. As a result of infusion the cross section area of the walls of the arteries was increased throughout the whole range of artery sizes, as evidenced by the shift of greatest frequency from the arteries of smaller area toward the arteries of greater area. Also, the total area of the walls of the arteries obtained from the ears infused with acetylcholine was much

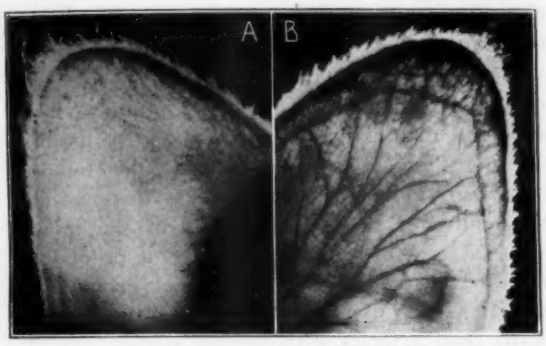
5. Mammalian Ringer's solution contains 0.900 Gm. of sodium chloride, 0.030 Gm. of potassium chloride, 0.025 Gm. of calcium chloride and 0.020 Gm. of sodium bicarbonate per hundred cubic centimeters.

6. Dr. Lewis D. Stevenson helped in the preparation and evaluation of the histologic slides.

greater (the average for 6 ears was 268 sq. cm. per hundred arteries per ear) than the area of the walls of the arteries from the control ears (the average for 6 control ears was 185.50 sq. cm. per hundred arteries per ear). This represents an increase in total area of 44 per cent over the control ears.

EXPERIMENTS WITH A VASOCONSTRICTOR SUBSTANCE

To ascertain whether a vasoconstrictor agent acts with equal promptness and to the same extent on thickened and on nonthickened arteries, the following experiments were performed. The vasoconstrictor agent, ergotamine tartrate, was chosen because it is an effective means of terminating an attack of migraine headache, and its use was, therefore, most relevant to this investigation.



Comparison of the effect of ergotamine tartrate on the control ear and on an ear infused previously for one hundred and twenty minutes with acetylcholine bromide (photograph taken by transillumination twenty-five minutes after injection of ergotamine tartrate).

A, control ear, showing striking vasoconstriction. Except for the marginal vessels, the blood vessels are barely visible. (The photograph of this ear, as compared with that of the infused ear (*B*), appears overexposed. This is because the exposure required for photographing the thickened, reddened infused ear was longer than was desirable for the thinner, pale control ear).

B, ear infused with acetylcholine bromide. The vasoconstriction was less evident, and the blood vessels were larger and more numerous than in the control ear.

Method.—Six cats were given infusions of acetylcholine bromide for two hours, as previously described, except that both ears were left in situ. Since the action of acetylcholine in the concentrations used is local and the agent is promptly destroyed, the ear on the infused side showed only the vasodilator effects of acetylcholine. The opposite, or control, ear retained its normal color and appearance. After two hours of infusion, ergotamine tartrate (0.007 mg. per kilogram) was injected into the femoral vein or subcutaneously, and the ears were inspected by transillumination and photographed.

Results.—Shortly after injection of ergotamine tartrate the control ear became pale and the vessels were notably constricted. The smallest vessels were no longer visible. In the infused ear the vasoconstriction began, or at least became noticeable, somewhat later. The time of vasoconstriction and the degree of constriction in the infused ear were variable. However, the infused ear remained redder than the control ear and its blood vessels significantly larger even after four hours! In 1 cat there was still a striking contrast between the arteries in the control ear and those in the infused ear after seven hours (figure).

COMMENT

From the data presented it is seen that cranial arteries exposed to the prolonged effect of the vasodilator agent acetylcholine bromide exhibit an increase in the thickness of the arterial walls. Thus, sustained dilatation of cranial vessels leads to transient structural changes. It is possible that the vasa vasorum in the dilated walls become more permeable and that the tissue spaces within the walls contain more fluid. The relation of these changes to clinical phenomena may be significant.

Dunning [7] collected the evidence concerning structural changes which he and others observed to be associated with attacks of migraine headache. In addition to prominent arteries, the defects outside the cranium include edema, ecchymosis, thrombosis and hemorrhage, and the defects within, thrombosis and hemorrhage. The facial edema and the results of hemorrhage may outlast the headache by many hours, or even days.

Changes in the appearance of capillaries have been observed during attacks of migraine headache.[8] These changes were attributed to swelling of the endothelial cells of the capillary wall [9] and to increased transudation.[8]

Kennedy [10] suggested that masses of fluid collected around intracranial blood vessels are responsible for both the migraine headache and the visual and other sensory disturbances. Kennedy's explanation is that the headache results from the rapidly formed "localized swellings" which stretch "agonizingly sensitive" meninges. This implies that during the attack of migraine the headache

7. Dunning, H. S.: Intracranial and Extracranial Vascular Accidents in Migraine, Arch. Neurol. & Psychiat. **48**:396 (Sept.) 1942.

8. Redish, W., and Pelzer, R. H.: Capillary Studies in Migraine: Effect of Ergotamine Tartrate and Water Diuresis, Am. Heart J. **26**:598, 1943.

9. Cohnheim, J. F.: Lectures on General Pathology, London, The New Sydenham Society, 1889.

10. Kennedy, F.: Migraine—A Symptom of Focal Brain Edema, New York State J. Med. **33**:1254, 1933.

precedes the visual defects because the fluid would be obliged to collect about the vessels before it could "irritate contiguous brain areas." As a matter of fact, however, visual disturbances usually precede the headache and end with its onset, or even before.

In short, there is no evidence that the edema associated with migraine is essential to the mechanism of either the preheadache or the headache phenomena. It may, however, modify the latter and manifest itself in other bodily effects, such as swelling of the face and extremities and disturbed urinary output.

The data thus far assembled have led us to the following formulation of the cranial mechanism concerned in the production of migraine: An initial local vasoconstriction of cerebral arteries produces visual and other sensory preheadache phenomena.[8] As these phenomena recede, vasodilator manifestations of headache appear. Sometimes the latter overlap the last traces of preheadache phenomena, and sometimes the headache begins after a short interval of freedom from symptoms. Rarely do the preheadache phenomena continue long after the headache has become established. The vasodilatation of certain cranial arteries, chiefly of one or another branch of the external carotid artery, gives rise to a throbbing, aching pain, which may be appreciably reduced by pressure on the common carotid artery, and sometimes on a superficial artery, and through the action of ergotamine tartrate. Vasodilatation when sustained during several hours leads to thickening or edema of the affected arterial wall and often to edema of adjacent tissue. Owing to transient thickening of their walls, the soft, readily collapsible arteries become rigid and pipelike. Further, the pulsating pain becomes a steady ache, and the artery itself becomes tender on palpation.

It has been demonstrated that ergotamine tartrate contracts a distended artery with thickened walls less promptly and completely than a normal one. Such differences in action indicate that ergotamine tartrate will be therapeutically most effective when administered soon after the onset of the attack of migraine headache.

CONCLUSIONS

After several hours of migraine headache changes in cranial arteries appeared. A distended temporal artery, for example, seems more prominent. It becomes more easily palpable through the skin, and, instead of being readily collapsible, is rigid and pipelike and is less easily compressed by the palpating finger. The nature of these alterations was studied by experimental induction of analogous changes in cats.

The structure of the arteries of the ears of 6 cats was studied after infusion for two hours of 10 cc. of mammalian Ringer solution containing 0.5 mg. of acetylcholine bromide per hundred cubic centimeters. Measurements demonstrated thickening of the arterial walls of the infused ears. Also, a vasoconstrictor agent, ergotamine tartrate, was observed to be less prompt and effective in constricting arteries with thickened walls than arteries with normal walls.

It is suggested that during attacks of migraine headache the cranial arteries involved may undergo similar changes after prolonged vasodilatation. Such changes may explain the rigid, pipelike texture of the arteries, the steady aching pain and the tenderness of these structures when headache has persisted for many hours. Also, these changes may explain the decreased ability of ergotamine tartrate to reduce promptly the intensity of prolonged headache.

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CEREBRAL INJURY BY BLUNT MECHANICAL TRAUMA

SPECIAL REFERENCE TO THE EFFECTS OF REPEATED IMPACTS OF MINIMAL INTENSITY; OBSERVATIONS ON EXPERIMENTAL ANIMALS

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PURPOSE OF INVESTIGATION

It has been suggested by several investigators that the effects of cerebral trauma may be cumulative. As far back as 1874 Koch and Filene [1] had shown that animals could be killed by repeated small blows on the head without showing any evidence of structural damage to the brain. Later Martland [2] recognized a peculiar condition occurring among prize fighters, which he named "punch drunk" and which he attributed to the repeated head punishments they had suffered while in the ring. Then Shaller, Tamaki and Newman [3] showed the apparent increase in vulnerability of the cerebral vessels induced by the application of repeated blows. More recently Denny-Brown and Russell [4] demonstrated that paralysis of respiration of increasing duration and rise of blood pressure occurred with successive blows and that concussion could be obtained readily by repetition of moderately severe blows.

In apparent contrast to these observations are those of Noble and associates [5] leading to the concept of "trauma resistance"; by gradually increasing the amount of trauma they found that animals could tolerate a number of blows fatal to a normal animal. In explanation of this, biochemical analysis of the blood and tissues by Neufeld, Toby and Noble [6] seemed to indicate that the resistance which develops as a result of repeated trauma involves a stabilization of metabolic processes, which are notably upset in the "non-resistant traumatized animal."

As further knowledge along this line seemed desirable, experiments were planned with the aim of seeing whether the disorders of function observed by other investigators could be correlated with demonstrable changes in the nervous system. More exactly, one of the main points with which I was concerned in my investigation has been that of studying, under controlled experimental conditions, the immediate and delayed effects of repeated moderately severe blunt impacts on the heads of animals. The repeated impacts were delivered in two ways—to some animals at relatively short intervals and to others at longer intervals, the total amount of trauma being the same for the two groups.

In relation to the mechanism of trauma, brain injuries have been said to occur in one of the two following ways: by distortion of the skull or by movements of the brain within the skull. In view of the possibility of different effects from the two mechanisms of trauma, the results of the repeated impacts, both in close succession and at longer intervals, were studied comparatively: in animals in which a distortion of the skull, even of slight degree, was likely to occur under the force of the impact, and in animals in which forces of acceleration were mainly involved.

A blunt impact on the animal's head while at rest was thought to realize the first condition, while the second condition was made possible by a procedure which permitted a rapid acceleration of the head and its sudden arrest by meeting a resistance.

MATERIAL AND METHODS

The albino rat was chosen as the experimental animal, in view of the facility with which changes in behavior can be detected in this animal. Mature male and female rats of the same strain and approximately similar weights,

From the Laboratories of the Medfield State Hospital.

This paper was read at the May 1944 meeting of the Massachusetts Psychiatric Society.

1. Koch, W., and Filene, W.: Beiträge zur experimentellen Chirurgie, Arch. f. klin. Chir. **17**:190, 1874.

2. Martland, H. S.: Punch Drunk, J. A. M. A. **91**:1103 (Oct. 13) 1928.

3. Shaller, W. F.; Tamaki, K., and Newman, H.: Nature and Significance of Multiple Petechial Hemorrhages Associated with Trauma of the Brain, Arch. Neurol. & Psychiat. **37**:1048 (May) 1937.

4. Denny-Brown, D., and Russell, W. R.: Experimental Cerebral Concussion, Brain **64**:93 (Sept.) 1941.

5. Noble, R. L., and Collip, J. B.: Quantitative Method for Production of Experimental Traumatic Shock Without Hemorrhage in Unanaesthetized Animals, Quart. J. Exper. Physiol. **31**:187 (Feb.) 1942. Noble, R. L.: Development of Resistance by Rats and Guinea Pigs to Amounts of Trauma Usually Fatal, Am. J. Physiol. **138**:346 (Jan.) 1943.

6. Neufeld, A. H.; Toby, C. G., and Noble, R. L.: Biochemical Findings in Normal and Trauma-Resistant Rats Following Trauma, Proc. Soc. Exper. Biol. & Med. **54**:249 (Nov.) 1943.

ranging from 180 to 205 Gm., were used. During the course of the experiments they were properly fed, with all precautions to avoid the complications derived from a dietary deficiency. The weight of the animals was taken at the beginning and at the end of the experiment and was checked periodically in the intervening period. The animals which did not die spontaneously as a direct consequence of the trauma were killed by inhalation of chloroform, dying within a few seconds; several control animals, submitted to inhalation of chloroform alone, did not show any demonstrable lesion in the nervous system. As soon as the animal was dead, the head was severed from the body and placed in a 10 per cent solution of formaldehyde U.S.P. in isotonic solution of sodium chloride. After forty-eight hours, the skull was opened, and the cerebrum, the cerebellum, the two parafloccular lobes and the cervical portion of the spinal cord were removed in one block. A thorough inspection of the abdominal and thoracic organs was made in all animals. This seemed to be indicated particularly in the rats in which the changes in the brain did not explain sufficiently the course of events following the trauma. When observation with the naked eye did not reveal any noticeable change on which to focus further studies the brain was divided into two blocks in a horizontal plane, from the tip of the olfactory lobes to the base of the fourth ventricle, the section passing through the basal nuclei at equal distances from the vault and the base. The lower block comprised the base of the cerebral hemispheres, the pons and the cerebellum, and the upper block, the vault of the cerebral hemispheres. One of the two blocks was embedded in paraffin, sectioned at different levels and stained with hematoxylin and eosin. From the other block frozen sections were made and stained according to the Cajal reduced silver method for nerve fibers, the Spielmeyer method for myelin sheaths, the Nissl method for nerve cells (cresyl violet) and the oil red O (pyridine solvent), sudan III and the Marchi method.

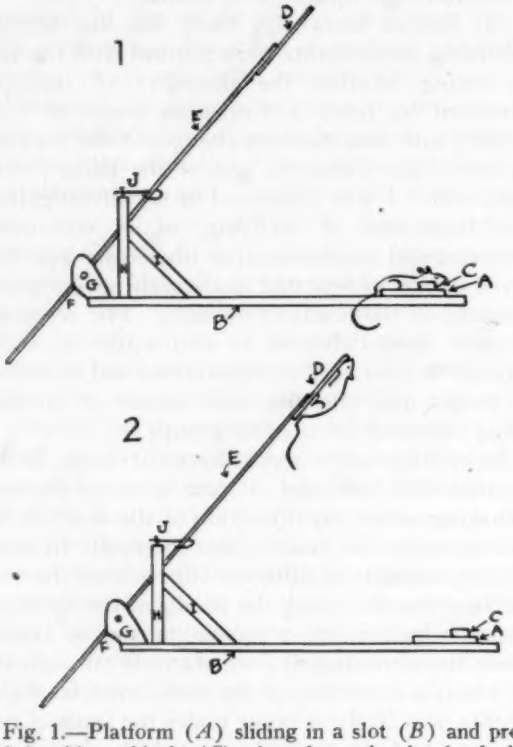

Fig. 1.—Platform (*A*) sliding in a slot (*B*) and provided with a block (*C*) shaped to the head of the animal; iron paddle (*D*), which can act either as a traumatizing agent or as a carrier of the animal; metal rod (*E*) passing through a revolving tumble block (*F*) set between two shoulders (*G*); upright block (*H*) reenforced by braces (*I*) and provided with a catch (*J*) to hold the rod and to release it suddenly.

As the traumatizing agent, an apparatus was devised and set up [7] which consisted of two fundamental parts (fig. 1, *1* and *2*): first, a rectangular wooden platform (*A*), sliding in a slot cut in the base (*B*) and provided with a block (*C*) shaped to the head of the animal; and, second, a rectangular iron paddle (*D*) of sufficient weight and size to act either as a blunt traumatizing agent, in the procedure of compression concussion (fig. 1 A), or as carrier of the animal, in the procedure of acceleration concussion (fig. 1, *2*). The metal rod (*E*), attached to the iron paddle, was passed through a revolving tumble block (*F*) set between two shoulders (*G*), so as to allow the length of the rod to be adjusted as desired; the tumble block was supported by an upright (*H*), reenforced by braces (*I*) and provided with a catch (*J*) to hold the rod and to release it suddenly.

The possibility of reproducing by this apparatus injuries of the type most commonly occurring in man as a result of accidental head trauma is easily seen. When the iron paddle was allowed to fall and strike the fixed head of the animal lying stationary on the platform, the condition was realized of a moving object striking the head at rest, whereas the method of having the animal fixed to the falling paddle and striking the head against the platform realized the condition of a fall from a height on to a hard surface.

In preliminary experiments on a large number of animals, in which the amount of trauma was gradually increased, the momentum of the force necessary to produce the desired degree of trauma and, correspondingly, of injury to the brain, was determined exactly. For each degree of trauma, the effects of blows of identical strength were studied comparatively with each of the two mechanisms—moving head against stationary object and moving object against stationary head. With application of either mechanism, the following degrees of trauma were produced:

1. A crushing injury, with fracture of the skull, extensive damage to the brain and its involucres and death within three hours—immediate lethal blow (mass, 973 Gm.; velocity at point of impact, 392.8 cm. per second).

2. A less severe but still fatal injury, with or without fracture of the skull, with cerebral damage of various degrees and delayed death, within from four hours to seven days—delayed lethal blow (mass, 744 Gm.; velocity at point of impact, 367 cm. per second).

3. A concussive blow, with transient loss of consciousness [8] and apparently complete recovery in vary-

7. Dr. E. K. Holt and Dr. E. K. Holt Jr. gave assistance in this undertaking.

8. The presence or absence or defect of consciousness is a matter for conjecture in the experimental animal which cannot give any reliable test response as a human being does. When clear evidence of paralysis of cerebral functions was not obtainable, the loss of the pupillary reflexes was taken as a basic criterion of concussion. The absence of fracture of the skull or of gross hemorrhagic or necrobiotic change in the brain, brain stem or cervical portion of the spinal cord on postmortem examination was included as an additional basic criterion of concussion.

ing periods (mass, 567 Gm.; velocity at point of impact, 345.7 cm. per second).

4. A subconcussive blow, the strength of which was insufficient to cause loss of consciousness or any other immediate or delayed ill effects (mass, 453.6 Gm.; velocity at point of impact, 330.9 cm. per second).

It was this blow of minimal intensity which was used in the investigation of cumulative effects of repeated trauma.

Precautions were taken that all animals should receive a trauma of the same momentum each time and that the heads of the animals should be struck in the same region. The occipitoparietal region was chosen because in the rat this area of the skull is thicker and less liable to fracture.

In summarizing the protocols of the experiments, I shall proceed according to the degree of trauma, from the most to the least severe, in the following order[9]: (1) immediate lethal trauma (12 animals); (2) delayed lethal trauma (15 animals); (3) concussive trauma—maximum sublethal trauma (68 animals); (4) subconcussive trauma, not repeated (30 animals); (5) subconcussive trauma, repeated (*a*) at long intervals (60 animals, and (*b*) in close succession (60 animals).

Special consideration will be given in this study to the observations arising from the experiments on the animals of group 5.

TABLE 1.—*Effects of Immediate Lethal Trauma*

Rat No.	Time of Death	Skull	Postmortem Observations—Brain		Other Observations
			Site of Impact	Contralateral Injury	
			Moving Head Against Stationary Object		
17	2 hr.	Fracture	Small areas of hemorrhagic softening in both occipital lobes		
22	Immediate	Fracture	Extensive contused lacerations, with indriven fragments of skull	Subarachnoid hemorrhage at base	
21	Immediate	Fracture	Extensive contused lacerations, occipitocerebellar region	Subarachnoid hemorrhage at base	
23	3 hr.	Fracture	Extensive contused lacerations, with indriven fragments of skull	Subarachnoid hemorrhage at base	
18	10 min.	Fracture	Extensive contused lacerations	Hemorrhages in pontobulbar region	
16	3 hr.	Fracture	Small area of hemorrhagic softening, left temporoparietal region	.....	Edema of lungs
			Moving Object Against Fixed Head		
77	Immediate	None	Extensive contused lacerations	Subarachnoid hemorrhage at base	
12	Immediate	Fracture	Diffuse subarachnoid hemorrhage; small areas of hemorrhagic softening in both frontal lobes	Subarachnoid hemorrhage at base	
5	5 min.	Fracture	Extensive contused lacerations.....	.....	Hemorrhagic erosions in stomach
6	8 min.	None	Extensive contused lacerations.....	.....	Hemorrhagic erosions in stomach
13	10 min.	Fracture	Extensive contused lacerations.....		
7	3 hr.	None	Diffuse subarachnoid hemorrhage; hemorrhagic softening, occipitoparietal region		

SURVEY OF EXPERIMENTS

IMMEDIATE LETHAL TRAUMA

Gross Observations.—The results of postmortem examination of the animals dying immediately or shortly after a crushing type of injury had been applied are graphically represented in table 1, and figure 2 shows the amount of cerebral damage suffered by the animals of this group. Fracture of the skull was found in almost all the rats, and in 2 animals (rats 22 and 23) fragments of skull were found deeply driven in the brain matter. Contusions and extensive bruising of the cortex, including several adjacent convolutions and involving to a considerable degree the underlying white substance, were outstanding features in all cases, without any differences that could be related to the mechanism of trauma. As Rand and Courville[10] have proposed, lesions of this type might be properly defined as "contused lacerations," thus emphasizing the role played by the blood flooding from the ruptured blood vessels in destroying and hollowing large areas of brain.

Contralateral injury, in the sense that a pole of the brain opposite the site of impact showed evidence of damage, was found in 1 animal only (rat 18); contralateral subarachnoid bleeding was, on the contrary, frequent, as the result of the tearing of the delicate vessels entering the base of the brain.

In this group an animal (rat 16) is included which died in the third hour, after the development of acute pulmonary edema. As the cerebral damage was rather limited in this animal, consisting of a small area of hemorrhagic softening in the left temporoparietal region, the impression was that the superseding pulmonary edema had

9. The animals used in the preliminary experiments (150 approximately) to establish the momentum of the force necessary to produce the different degrees of trauma are not included.

10. Rand, C. W., and Courville, C. B.: Histologic Changes in the Brain in Cases of Fatal Injury to the Head: V. Changes in the Nerve Fibers, Arch. Neurol. & Psychiat. **31**:527 (March) 1934.

rendered fatal what otherwise would have been a reparable injury to the brain.

Among the subsidiary findings, the presence of blood in the stomachs of 2 animals (rats 5 and 6) deserves mention. In both animals the gastric mucosa showed a scattering of tiny hemorrhages, which had a tendency to aline themselves along the crests of the gastric plicae. The hemorrhages were in general superficial, and as the mucosa was not depressed or otherwise altered, the resulting pattern was that of a simple hemorrhagic change.

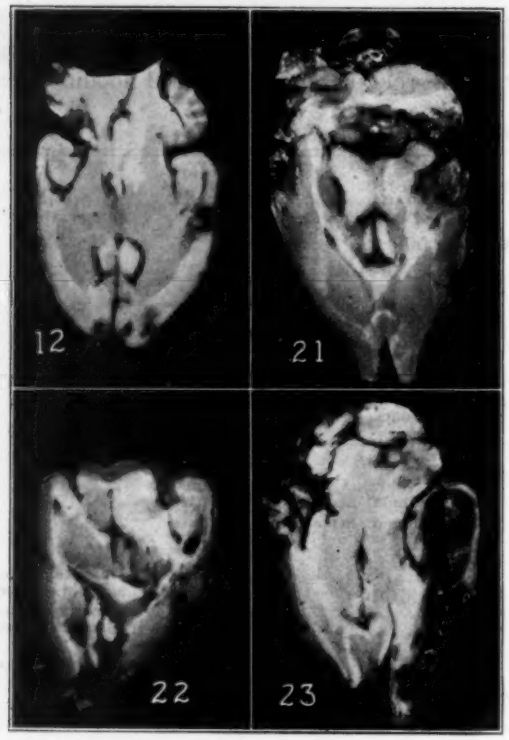

Fig. 2.—Horizontal sections of the brains of 4 animals which died shortly after a crushing type of injury (immediate lethal trauma), showing extensive contused lacerations. Rats 21, 22 and 23 struck the moving head against the stationary object; rat 12 was struck by the moving object on the stationary head. Fracture of the skull was a constant finding in all cases, and in 2 animals (rats 22 and 23) fragments of skull were found driven deeply in the brain matter.

With the exception of 1 animal that received the blow without showing loss of consciousness but shortly thereafter became comatose and died in the third hour, all the animals of the group were made unconscious at the time of the trauma and did not recover before death.

Microscopic Observations.—As one would expect, no evidence of progressive change was seen in the microscopic sections of the brains of the animals dying outright after the trauma. At the site of the hemorrhages there was almost complete obliteration both of cells and of fibers; and when fibers were still recognizable, they appeared twisted, fragmented and widely separated one from another by the interposed extravasated blood.

Progressive changes in nerve fibers, on the other hand, were already present in the animals surviving the trauma from two to three hours. In the hemorrhagic areas some of the nerve fibers stained poorly; others were deeply impregnated, and still others appeared to be thickened, with interruptions which at times resolved themselves into granular formations (fig. 3 *A*). Granular disintegration and twisting of fibers, with peculiar zigzag figures and terminal swelling of the ends of the fragmented fibers (bulbs of retraction), were also noticeable in the immediate vicinity of the hemorrhagic areas and at times in remote areas of the brain, otherwise undamaged (fig. 3 *B*). The lesions in the axis-cylinders were accompanied by evidence of disintegration of the myelin sheaths, which already at the second hour displayed varicose swelling, moniliform thickening, with reabsorption in areas, and formation of ellipsoids and fatty droplets (fig. 3 *C*). Clublike formations at the ends of the degenerated portions of interrupted fibers were noticeable in the myelin preparations, and they seemed to correspond to the bulbs of retraction of the fragmented axons in the silver-impregnated sections.

All these findings are in agreement with previous observations by other authors (Jakob,[11] Pfeifer,[12] Schwartz and Fink,[13] Rand and Courville,[10] Greenfield,[14] Hassin[15]) and lend further support to the recent conclusion of Rowbotham[16] that "demonstrable changes in neurons, other than in contusional areas, can always be found following fatal (head) injuries."

11. Jakob, A.: Ueber die feinere Histologie der sekundären Faserdegeneration in der weissen Substanz des Rückenmarks, in Nissl, F., and Alzheimer, A.: Histologie und Histopathologie. Arbeiten über die Grosshirnrinde, Jena, Gustav Fischer, 1912, vol. 5, p. 1; Experimentelle Untersuchungen über die traumatischen Schädigungen des Zentralnervensystems, ibid., vol. 5, p. 182.

12. Pfeifer, B.: Ueber die traumatische Degeneration und Regeneration des Gehirns erwachsener Menschen, J. f. Psychol. u. Neurol. **12**:96, 1908.

13. Schwartz, P., and Fink, L.: Morphologie und Entstehung der geburtstraumatischen Blutungen im Gehirn und Schädel der Neugeborenen, Ztschr. f. Kinderh. **40**:427, 1925.

14. Greenfield, J. G.: Some Observations on Cerebral Injuries, Proc. Roy. Soc. Med. **32**:43 (Nov.) 1938.

15. Hassin, G. B.: General Pathological Considerations in Brain Injury, in Brock, S.: Injuries of the Skull, Brain and Spinal Cord, Baltimore, Williams & Wilkins Company, 1940, chap. 2.

16. Rowbotham, G. F.: Acute Injuries of the Head, Baltimore, Williams & Wilkins Company, 1942.

Fig. 3.—*A*, twisting and fragmentation of nerve fibers in a subcortical area of contused laceration. The animal, rat 7, died three hours after a severe blow on the stationary head which had left the skull intact (immediate lethal trauma). Cajal stain; ocular 4; objective 10.

B, thickening, spiroid course and splitting and fragmentation of nerve fibers in a portion of brain, apparently undamaged, at some distance from the area of contusion shown in *A*. Cajal stain; ocular 4; objective 10.

C, from a section at a level corresponding to that of sections *A* and *B*, showing severe disintegration of myelin with formation of ellipsoids and fat droplets. Spielmeyer stain; ocular 4; objective 40.

In the study of the sections in this figure, and of those in figures 4, 9, 10, 11, 12, 13 and 14, a Bausch & Lomb microscope was used.

DELAYED LETHAL TRAUMA

The longer period of survival, from four hours to seven days, of the animals of this group, which were submitted to a trauma of less intensity, and the lesser magnitude and depth of the cerebral damage justify a separate description. As is graphically represented in table 2, only 3 animals showed evidence of fracture of the skull. At the site of impact the cerebral damage varied from a more or less extensive subarachnoid hemorrhage to contused laceration of the brain substance, involving at times several contiguous convolutions. Opposite the zone of impact evidence of contralateral injury was found in 4 rats; in 2 animals the damage consisted of subarachnoid hemorrhage, while in 2 others a dissemination of tiny hemorrhages was noticeable in the pons and the bulbar region. With respect to the two mechanisms of trauma, no differences were noticed in the apparent effects with blows of equal intensity.

In 7 of 15 animals, postmortem examination of the brain failed to reveal any change that could be detected with the naked eye. The examination of these animals was extended to large portions of the spinal cord, which also appeared grossly intact. In 2 of these rats acute bilateral pulmonary edema accounted, very likely, for the sudden death, which occurred at the eighth and the twenty-fourth hour after an apparently good recovery from a short period (five to ten minutes) of unconsciousness following the trauma. A condition of shock was suspected in 2 other animals which lost consciousness after the trauma, did not regain it completely and died at the fourth and fifth hours respectively, showing pronounced congestion of the abdominal organs. In the remaining 3 animals the postmortem observations did not offer any plausible explanation to account for the fatal outcome.

Microscopic Observations.—It was mainly on the brains of these 7 rats that the histologic study was focused. Changes in the nerve cells, axis-cylinders and myelin sheaths, which at times represented the only signs of local damage, less frequently accompanied by evidence of tissue edema, were revealed in the microscopic sections from all these apparently undamaged brains. Such changes were not diffuse but were focal in distribution, areas which appeared entirely normal alternating in the same field with others displaying more or less severe disintegration of neurons. This disintegration could be followed in its progressive stages according to the period of survival of the animal. In the animals which died from the fourth to the eighth hour the cortical nerve cells here and there appeared swollen, with huge cytoplasmic vacuoles which had a tendency to aline themselves at the periphery of the cell bodies. The apical dendrites were thickened, either diffusely or in limited tracts, and tortuous, with curvatures of varying depths and with a corkscrew twisting that contrasted sharply with the linear course of undamaged axis-cylinders nearby. Other cells showed absence of expansions (aneuritic cells), whereas still others

TABLE 2.—*Effects of Delayed Lethal Trauma*

Rat No.	Time of Death	Skull	Postmortem Observations—Brain		Other Observations
			Site of Impact	Contralateral Injury	
			Moving Head Against Stationary Object		
72	4 hr.	.....	Not remarkable.....	.....	Congestion of abdominal organs
71	5 hr.	.....	Not remarkable.....	.....	Congestion of abdominal organs
1	15 hr.	.....	Not remarkable.....	.....	.....
22	6 hr.	Fracture	Contused laceration of occipitotemporal region	Subarachnoid hemorrhage at base	
23	4 hr.	Fracture	Contused laceration of occipitocerebellar region	Subarachnoid hemorrhage at base	
30	8 hr.	.....	Not remarkable.....	.....	Pulmonary edema
2	24 hr.	.....	Not remarkable.....	.....	Pulmonary edema
11	24 hr.	.....	Subarachnoid hemorrhage.....	Hemorrhages in pontobulbar region	Pulmonary edema
9	5 days	.....	Small area of softening in frontal region		
8	7 days	.....	Occipital subarachnoid hemorrhage	.....	Hemorrhagic erosions in stomach
			Moving Object Against Stationary Head		
95	4 hr.	Fracture	Diffuse subarachnoid hemorrhage	Hemorrhages in pontobulbar region	
78	19 hr.	.....	Diffuse subarachnoid hemorrhage		
80	3 days	.....	Not remarkable.....		
85	5 days	.....	Not remarkable.....		
81	5 days	.....	Occipitotemporal subarachnoid hemorrhage		

exhibited granular tracts which outlined the course of the disintegrated dendrites. Changes of the same type were seen in the medullated axons, which in some places displayed varicose swelling or fragmentation, with bizarre end bulbs of various sizes and occurring mostly as small balls or spirals. The changes in the axis-cylinders were accompanied by changes of corresponding severity in the myelin sheaths, which had a moniliform appearance, narrow segments alternating with fusiform or ovoid swellings of various sizes. Evidence of more advanced disintegration of myelin was shown by the animals surviving the effects of the trauma longer—from nineteen hours to seven days. It consisted of conglomerates of fat droplets, which had a tendency to assume a linear distribution along the damaged axons. The latter appeared mostly as granular remnants with balls here and there, at times free and at times still attached to the ends of the degenerated portions of interrupted fibers. When the evidence of damage was most severe, bizarre-shaped scavenger cells, containing fat globules, were noticeable.

CONCUSSIVE TRAUMA (MAXIMUM SUBLETHAL TRAUMA)

Sixty-eight animals received a single blow on the head that made them unconscious for a period varying from ten seconds to fifteen minutes, followed by recovery. These 68 animals were divided into two groups, half being made to strike the moving head against the stationary object and the other half being struck on the stationary head by a force of exactly the same momentum. With blows of identical strengths, no differences were noted in the effects with the two mechanisms of trauma.

Some of the animals were killed shortly after the trauma, from one hour to seventy-two hours, in order to detect any early organic changes. Others were kept under observation for two months and then killed. During this period the great majority of the animals did not reveal any evidence of abnormal psychomotor behavior. Only 4 rats showed decreased activity and progressive loss of weight, estimated at the end of the experimental period to be about 30, 38, 42 and 45 Gm. respectively.

Microscopic Observations.—In all animals but 1, in which petechial hemorrhages were found both in the pons and in the bulbar region, gross inspection of the brains, and even of the sections stained with hematoxylin and eosin, failed to reveal any demonstrable changes except for occasional vascular engorgement and doubtful signs of edema of the brain matter. Changes in nerve cells, axis-cylinders and medullary sheaths were seen, however, when the stains proper for the nerve tissue elements were applied.

In the Cajal silver-stained preparations of the brains of animals killed one and two hours after the trauma, the apical dendrites appeared thickened, with a somewhat spiral course and at times a definite corkscrew shape (fig. 4 *B*). The corresponding nerve cells in the Nissl preparations showed loss of clearness of cell outlines, swollen cytoplasm and tigrolysis, with displacement of the nucleus to the periphery of the cell body (fig. 4 *A*). These changes were not diffuse, as groups of cells with evidence of damage alternated with others displaying normal cellular patterns and axis-cylinders pursuing their usual straight course. The same type of focal change was displayed by the medullated axons, some of which appeared poorly impregnated, varicose and swollen, in contrast to other axons which were overstained with the reduced silver (fig. 4 *C*). Still other fibers showed twisting; and when two or three of these twisted fibers lay close together, they gave rise to peculiar loops and spirals, to which corresponded a moniliform thickening or a fusiform swelling of variable size in the myelin-stained preparations (fig. 4 *D*).

More advanced myelin disintegration and neurolysis were noticeable in the animals killed from the fourth to the seventy-second hour. Conspicuous corkscrew twisting of the axis-cylinders was still recognizable in sparse areas, but more frequently in these animals the location of the axis-cylinders was indicated by irregular fragments, at times ending in blunt-tipped bulbs, and by tail-like rows of disappearing granules. The changes in the axis-cylinders corresponded fairly well, both in severity and in distribution, to those in the myelin sheaths. Individual myelin sheaths in the process of disintegration appeared swollen, thickened and fragmented, with reabsorption in areas and resolution into round, oval or irregularly shaped fat globules. The fat globules lay for the most part free in the tissue; to a less extent they were contained within compound granular corpuscles.

Of the animals killed after two months, none showed at postmortem examination any grossly detectable evidence of the previous trauma. In the majority of the animals microscopic study of the sections also failed to reveal any significant change. Microscopic examination of the brain sections of the 4 rats which had shown decreased activity and progressive loss of weight after the trauma revealed, on the contrary, rarefaction of nerve cells in disseminated zones of the cerebral cortex and small areas of demyelination in the subcortical white matter, with almost complete obliteration of axis-cylinders and evidence of free

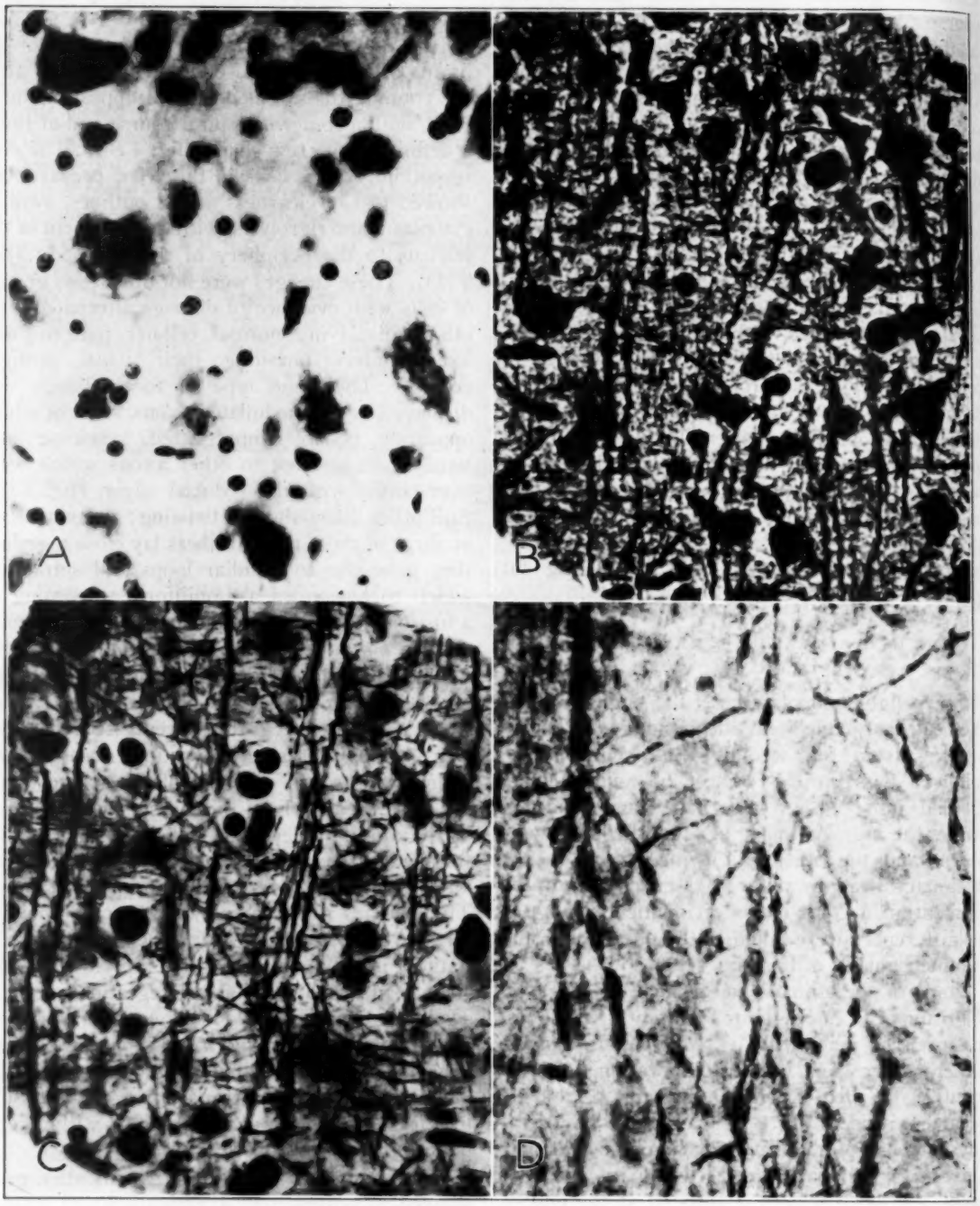

Fig. 4.—*A*, swelling, tigrolysis and pericellular edema of cortical nerve cells in a rat (no. 4) killed one hour after a concussive blow of moderate intensity (immediate lethal trauma)—moving head struck against stationary object—which had made it unconscious for five minutes and had left the skull and brain apparently intact. Nissl stain; ocular 6; objective 40.

B, from a Cajal preparation at a level corresponding to that of *A*, showing pronounced thickening, corkscrew twisting and occasional fragmentation of the apical dendrites. Ocular 4; objective 40.

C, medullated axons in the white matter of the perithalamic region, showing flexuous aspect, overstaining and at times spiroid course and fragmentation. Cajal stain; ocular 4; objective 40.

D, swelling, moniliform thickening and incipient breaking down of myelin sheaths in the same area of the brain. A few fairly well preserved myelin sheaths are still recognizable in the field. Spielmeyer stain; ocular 6; objective 40.

balls in the corresponding areas. In the parts that were damaged there was hyperplasia of astrocytes, which did not seem to be accompanied with an appreciable increase of glial fibers.

SINGLE SUBCONCUSSIVE TRAUMA

The term subconcussive is here applied to a trauma of such minimal strength as to be insufficient to cause loss of consciousness or any other apparent immediate or delayed effect in a normal animal. Thirty rats, divided into two equal groups, were submitted to this trauma; in one group the moving head was made to strike the stationary object and in the other the moving object struck the fixed head. All animals were killed at intervals of from one hour to forty days after the trauma, and none of them showed either gross or microscopic evidence of lesions.

REPEATED SUBCONCUSSIVE TRAUMA AT LONG INTERVALS

Cumulative effects, as revealed by temporary loss of consciousness, at times followed by death or by persisting functional disorders,[17] were shown with a certain frequency when a trauma of the same strength as the one used in the previous experiment was repeated at intervals of from two to six days, with a total of fifteen blows delivered in a fifty day period. As shown in table 3, both groups of animals, the rats striking the moving head against the stationary object (A) and the rats with the stationary head struck by the falling hammer (B), showed evidence of ill effects under the increasing trauma, but the frequency differed in the two groups. Already at the third and the fourth blow, respectively, in the two groups a few animals began to lose consciousness, and their number increased steadily under the successive blows. At the end of the experiment 57 per cent of the animals of group A had been made unconscious; of these, 7 per cent showed persisting functional disorders, and 17 per cent died as a direct consequence of the trauma. The incidence of ill effects was somewhat lower in the animals of group B, with only 40 per cent showing temporary loss of function, none dying and 10 per cent showing persisting functional disorders, while the majority, 60 per cent, went through the entire experimental period without displaying any immediate or late effects of the repeated trauma.

In most instances, once the animal had begun to lose consciousness, concussive effects occurred with each successive blow. A limited number of animals, however, which had been made unconscious by a previous blow failed to reveal any immediate ill effects from the next blow, to become unconscious again at a later blow.

The period of unconsciousness varied in the different animals each time from transient loss of the corneal reflexes to a more extensive paralysis of functions, lasting from a few minutes up to one hour. There was no apparent correlation between the number of blows and the duration of the state of unconsciousness.

Of the symptoms of abnormal behavior occasionally developing as the result of the repeated trauma, the most apparent was an unusual stiffness in the posture of the animal, interrupted at times by spells of more or less generalized trembling. The animals responded slowly to all types of external stimulation and often refused to eat, the result being a rapid decrease in body weight. When made to walk, they showed unsteady gait and a somewhat uncertain equilibrium, and at intervals flopping of one leg. Later, distinct dragging of the legs developed, with general slowing down of muscular movements. In general, once these symptoms had started, they showed a tendency to progress rapidly and then to remain stationary, having reached a certain level (observations up to the one hundred and twentieth day). All animals affected in this way had been made unconscious in the course of the experiment. No definite correlation could be seen, however, between the duration of the loss of consciousness at the moment of impact and the symptoms of abnormal behavior developing later, as they were seen both in the animals which had shown immediate evidence of severe concussion and in animals in which the only sign of concussion had consisted in transient loss of corneal reflexes.

IN CLOSE SUCCESSION

In contrast to the animals of the previous experiment, which received the blows at long intervals, the animals in this experiment received the blows in close succession, one after another, at intervals of approximately one minute. In this experiment, at the first evidence of concussion the animal was released, and in no case was the experimental period protracted beyond fifteen blows. As seen in table 4, a small number of animals in each of the two groups (A, the rats striking the moving head against the stationary object, and B, the rats with the fixed head struck by a moving object) were already unconscious at the end of the fifth blow, additional animals being made unconscious with the succeeding blows. At the end of the experimental period

17. The words "functional disorder" are used here in their proper sense, to indicate a "disorder of function of the brain." They are not used in the common clinical sense, in which they often have a "psychogenic" connotation.

73 per cent of the animals of group A had been made unconscious, in contrast to 40 per cent of group B. Most of the animals made unconscious* under the repeated trauma showed a prompt and apparently complete recovery; a few fatalities occurred, however, in both groups of animals, with an incidence of 17 per cent in group A and of 7 per cent in group B, while in a few others persisting symptoms of functional disorders developed, namely, in 13 and 10 per cent, respectively, of the two groups. These symptoms, which were fairly similar to those described in the previous experimental groups, appeared shortly after the trauma in some animals and several days or weeks later in other animals. All animals displaying persisting evidence of abnormal behavior had received a large number of blows. This was true, for instance,

TABLE 3.—*Effects of Repeated Subconcussive Trauma Given Two to Six Days Apart.**

Rat No.	Number of Blows 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Persisting Functional Disorders
A. Moving Head Against Stationary Object																
138	—	—	U-5″†	—	U-15″	U-2′	U-20″	U-4′	U-5′	U-10″	U-2′	U-5′	U-4′	U-20′	U-45′	
139	—	—	—	U-2″	U-10″	—	U-8″	U-Died at 24 hours								
33	—	—	—	U-10′	U-1′	U-2′	U-2′	U-4′	U-10′	U-20′	Procedure discontinued.....					Began at 7th blow
40	—	—	—	—	U-2″	U-5″	U-2′	U-1′	Died in 1 hour							
36	—	—	—	—	U-4″	U-2′	U-Died in 1 hour									
41	—	—	—	—	U-2″	U-3″	U-3″	U-10′	U-15′	U-Died in 2 hours.....						Began at 8th blow
34	—	—	—	—	—	U-3″	U-2″	U-1′	U-2″	U-10′	U-4′	—	U-10′	U-18′	U-60′	
27	—	—	—	—	—	U-3″	U-4″	U-5″	U-10′	U-20″	U-5′	U-4′	U-3′	U-12′	U-30′	
35	—	—	—	—	—	—	U-2′	U-Died at 24 hours								
32	—	—	—	—	—	—	—	U-3′	U-7′	U-15′	U-8′	U-20′	U-5′	U-2′	U-10′	
38	—	—	—	—	—	—	—	U-2″	U-3″	U-1′	—	U-4′	U-7′	U-5′	U-12′	
29	—	—	—	—	—	—	—	—	U-2″	U-2′	U-3′	U-7′	—	U-10′	U-5′	
39	—	—	—	—	—	—	—	—	—	U-2′	U-1′	—	U-3′	U-5′	U-6′	
31	—	—	—	—	—	—	—	—	—	U-3′	—	—	U-6′	U-4′	U-8′	
131	—	—	—	—	—	—	—	—	—	U-8′	U-2′	U-5′	U-40″	P-7′	U-10′	
141	—	—	—	—	—	—	—	—	—	—	—	—	—	U-10′	U-60′	
133	—	—	—	—	—	—	—	—	—	—	—	—	—	—	U-5′	
42	—	—	—	—	—	—	—	—	Procedure discontinued.....							Control
37	—	—	—	—	—	—	—	—	—	—	Procedure discontinued.....					Control
43																
134																
135																
136																
137																
140	No immediate or delayed effects (15 blows)															
142																
132																
44																
49																
143																
B. Moving Object Against Stationary Head																
168	—	—	—	U-5′	U-3′	—	U-10″	U-5′	U-20″	U-6′	Procedure discontinued.....					Began at 5th blow
89	—	—	—	U-5″	—	—	—	U-10″	U-5′	U-20′	Procedure discontinued.....					Began at 9th blow
91	—	—	—	—	U-5″	—	—	U-1′	U-2′	U-10′	—	U-30″	U-5′	U-8′	U-12′	
171	—	—	—	—	U-5″	—	U-2′	U-5′	U-30″	U-10′	—	—	U-1′	U-15′	U-13′	
177	—	—	—	—	U-10″	U-2′	—	U-10′	U-15′	U-5′	—	U-20″	U-2′	U-30″	U-6′	
184	—	—	—	—	—	—	—	U-10″	U-50″	U-15′	U-3′	—	U-7′	U-2′	U-5′	
186	—	—	—	—	—	—	—	U-20″	U-1′	U-5′	U-2′	U-4′	U-1′	U-10′	U-20′	
88	—	—	—	—	—	—	—	U-3″	U-5′	U-60′	Procedure discontinued.....					Began at 10th blow
163	—	—	—	—	—	—	—	—	U-10″	U-5′	U-40″	U-2′	U-5′	—	U-10′	
164	—	—	—	—	—	—	—	—	U-15″	U-20′	—	U-4′	U-6′	U-50″	U-8′	
182	—	—	—	—	—	—	—	—	—	—	—	U-20″	—	U-2′	U-3′	
173	—	—	—	—	—	—	—	—	—	—	—	—	—	U-5′	U-9′	
90	—	—	—	—	—	—	—	—	—	—	Procedure discontinued.....					Control
87	—	—	—	—	—	—	—	—	—	—	Procedure discontinued.....					Control
86																
165																
166																
167																
169																
170																
172																
174																
175	No immediate or delayed effects (15 blows)															
176																
178																
179																
180																
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183																
185																

C. The Two Mechanisms of Trauma

Animals Which Were Made Unconscious, Had Persisting Functional Disorders or Died, with the Two Mechanisms of Trauma

Procedure	Unconsciousness	Persisting Functional Disorders	Death (Within 29 Days)	No Apparent Effects
Moving head, stationary object.....	57%	7%	17%	43%
Moving object, stationary head.....	40%	10%	0	60%

* In this table, and in table 4, the data for the blow employed were as follows: mass, 453.6 Gm.; velocity, 330.9 cm. per second; kinetic energy, 1.83.

† U indicates unconsciousness, measured in seconds or minutes.

TABLE 4.—*Effects of Subconcussive Trauma, Repeated in Close Succession*

Immediate and Late Results	No. Blows	No. Animals	Total
A. Moving Head Against Stationary Object			
Unconsciousness....	1- 5	3	22 (73%)
	6-10	8	
	11-15	11	
Late functional disorders			4 (13%)
Death (within 29 days)...			5 (17%)
No apparent effects			8 (27%)
B. Moving Object Against Stationary Head			
Unconsciousness....	1- 5	2	12 (40%)
	6-10	3	
	11-15	7	
Late functional disorders			3 (10%)
Death (within 29 days)...			2 (7%)
No apparent effects			18 (60%)

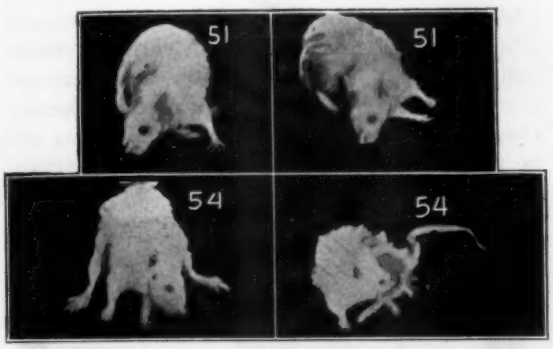

Fig. 5.—Locomotor disorders in 2 rats, as they appeared ten days after the trauma. Rat 51 had received thirteen subconcussive blows in close succession (moving head struck against stationary object) and was unconscious for about ten minutes. Rat 54 received fifteen subconcussive blows in close succession (moving object striking against stationary head) and was unconscious for a few seconds. Evidence of psychomotor disorders developed in both animals a few days after the trauma.

of the 2 rats, 51 and 54, shown in figure 5, which received thirteen and fourteen blows, respectively —rat 51 by the procedure of striking the moving head against the stationary object and rat 54 by the procedure of the moving object striking the stationary head. Rat 51 was unconscious for about ten minutes; rat 54, for a few seconds. Both began to show unsteady gait and general slowing down of muscular movements a few days after the trauma. One died at the twenty-ninth day of the experiment, and the other was killed at the thirty-fifth day because it was extremely emaciated and unable to eat. The symptoms presented by these 2 animals, and by the others similarly affected, are suggestive of the symptoms described in human beings as among the late results of repeated head injuries apparently of a minor type (Martland [2]); the comparison, however, for obvious reasons, cannot be pursued further.

The effects of repeated subconcussive blows in close succession—one minute apart—and at intervals of two to six days, under the two mechanisms of trauma are compared in table 5. With respect to the interval between blows no remarkable differences are seen in the group of animals struck by the moving object on the stationary head. With the other mechanism of trauma, the animals which had received the blows in close succession showed a higher incidence of unconsciousness than the animals which had received the repeated trauma at longer intervals.

TABLE 5.—*Comparative Effects of Repeated Subconcussive Blows Delivered in Close Succession and at Intervals According to the Two Mechanisms of Trauma, as Shown by the Percentage of Animals Which Were Made Unconscious, Showed Persisting Functional Disorders or Died (Within Twenty-Nine Days)*

Procedure	Unconsciousness	Persisting Functional Disorders	Death (Within 29 Days)	No Apparent Effects
A. Moving Head Against Stationary Object				
Blows repeated in close succession.....	73%	13%	17%	27%
Blows repeated at intervals (2-6 days)..	57%	7%	17%	43%
B. Moving Object Against Stationary Head				
Blows repeated in close succession.....	40%	10%	7%	60%
Blows repeated at intervals (2-6 days)..	40%	10%	0	60%

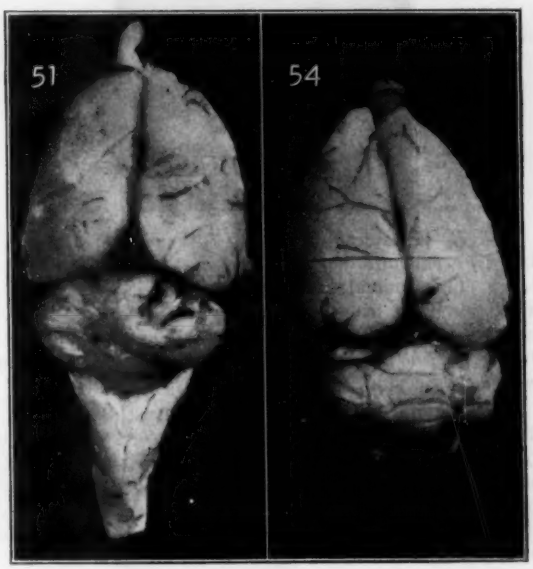

Fig. 6.—Gross appearance of the brains of 2 animals (rats 51 and 54) which had displayed pronounced psychomotor disorders during life, as shown and described in figure 5. No evidence of abnormality is seen in either brain.

Postmortem Observations.—In an investigation of a possible relation between the symptoms presented by the animals during life and the postmortem changes, the question arises whether the animals that stood the repeated trauma, given either at long intervals or in close succession, without showing any apparent immediate or late ill effects suffered an amount of damage different from that exhibited by the animals which were made unconscious, once or repeatedly, or which displayed any other evidence of post-traumatic functional disorders.

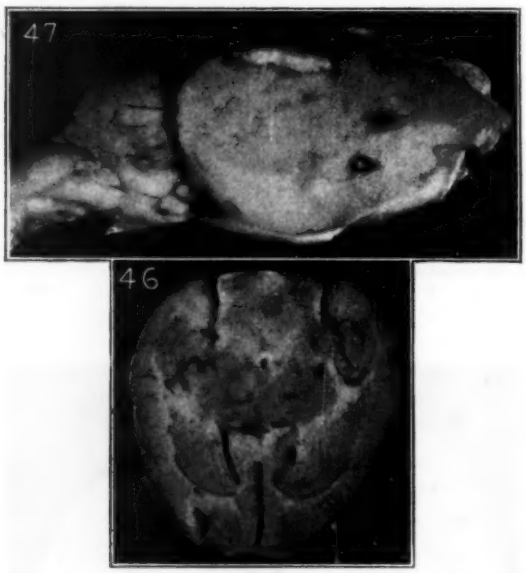

Fig. 7.—*A*, lateral view of the brain of rat 47, showing two punctate hemorrhages in the right temporal lobe. This animal was unconscious for five minutes after receiving fifteen blows in close succession (moving head struck against stationary object) and died twenty-four hours later, of acute generalized pulmonary edema. The skull was intact.

B, horizontal section of the brain of rat 46, revealing dissemination of tiny petechial hemorrhages of the ring type both in the cortex and in the white matter. This animal was unconscious for twenty minutes after receiving fifteen blows in close succession (moving head struck against stationary object) and died forty-eight hours later. The skull was intact.

In order to investigate as far as possible eventual correlations between disorders of function and histologic changes, when an animal which had shown such disorders died or was killed another animal apparently unaffected by trauma of identical type, intensity and frequency was killed at the same time, and the histologic sections of the brains of the 2 animals were closely compared at corresponding levels. As far as could be judged from the material examined, in most of the animals there was a certain relation between the response to the trauma during life and the amount of cerebral damage, as the latter appeared to be least severe in the animals which were clinically unaffected and became progressively more severe as the animals were made unconscious repeatedly, manifested persisting functional disorders or died as the result of the repeated trauma.

In the great majority of the animals postmortem examination did not reveal any deviation from the normal that could be detected with the naked eye. This is true, for instance, of the 2 brains represented in figure 6, from rats 51 and 54, which had displayed conspicuous psychomotor disorders during life. Gross evidence of injury to the brain, however, was seen in a few animals—in 7 of 120 animals submitted to the repeated trauma. In 1 animal, rat 46 (fig. 7), which was unconscious for about twenty minutes after receiving fifteen blows in close succession and died four days later, after an apparently good recovery, dissemination of petechial hemorrhages of the ring type, both in the cortex and in the white matter, was noted on horizontal section of the brain, the bleeding points being most numerous in the white substance; there were concomitant hemorrhagic erosions in the

Fig. 8.—*A*, superior view of the brain of rat 92, showing extensive subarachnoid hemorrhages in the temporoparietal regions of both hemispheres, in the cerebellum and in the brain stem. The animal was unconscious for about one hour after receiving nine subconcussive blows in close succession on the stationary head and died seven days later. There was no evidence of fracture of the skull.

B, superior view of the brain of rat 94, showing a thin layer of clotted blood between the cerebellum and the meninges. This animal was made unconscious by fifteen blows in close succession on the stationary head and died four days later. The skull was intact.

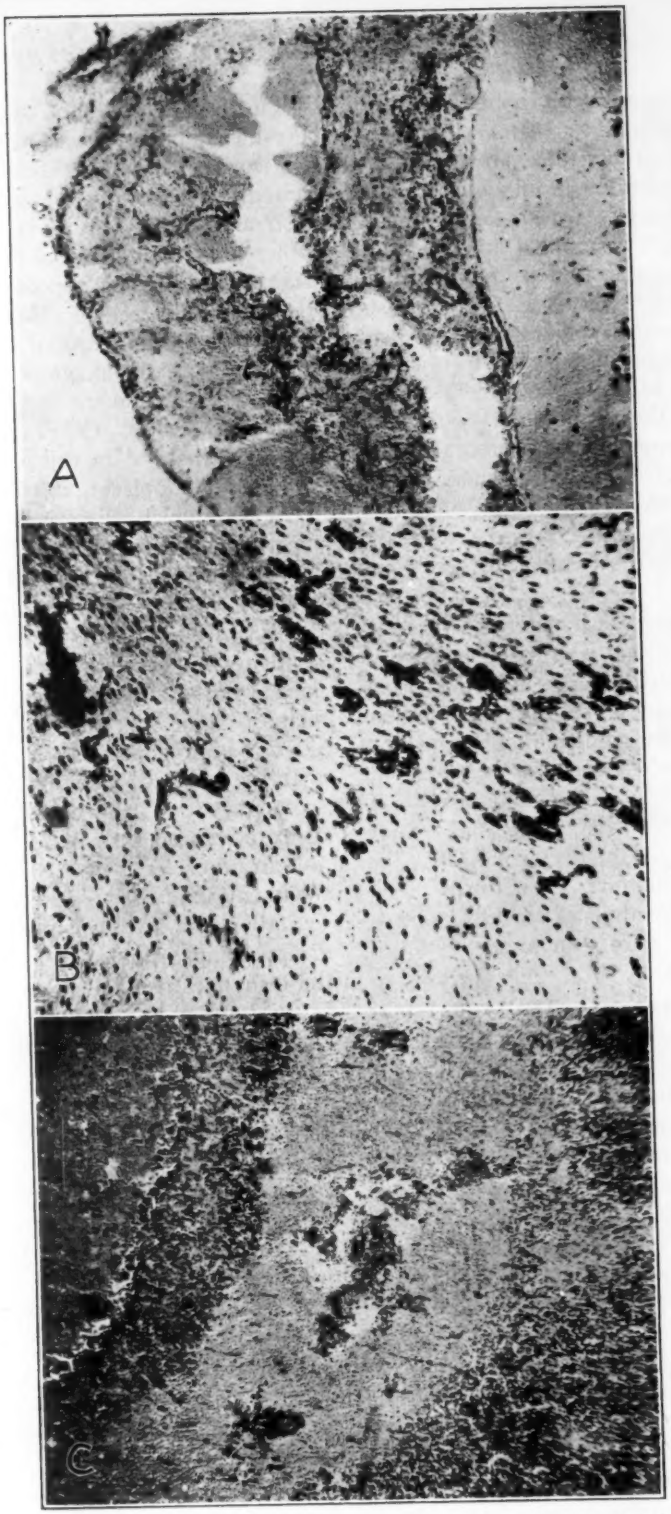

Fig. 9.—*A*, subarachnoid hemorrhage encroaching on the tip of the right frontal lobe. There was no evidence of skull fracture. The animal, rat 41, received ten subconcussive blows at long intervals (moving head struck against stationary object) and was repeatedly made unconscious from the fifth to the tenth blow. After the last blow the rat did not regain consciousness and died twenty-four hours later. Starting at the eighth blow it showed persisting slight psychomotor disorders. Ocular 4; objective 10.

B, recent hemorrhagic extravasations in the cortex of the occipital region of rat 27, which had received fifteen subconcussive blows at long intervals and was repeatedly made unconscious, starting at the sixth blow; it was killed two hours after the last blow. No evidence of fracture of the skull was found. Ocular 4; objective 10.

C, small hemorrhagic effusions in the white matter of the cerebellum. The animal, rat 38, had been made repeatedly unconscious by subconcussive blows at long intervals (moving head struck against stationary object) and was killed twenty-four hours after the last blow. The skull was intact. Ocular 4; objective 10.

gastric mucosa in this animal. In another animal, rat 47 (fig. 7), which had a history like that of the preceding animal but died in twenty-four hours, of acute generalized pulmonary edema, two punctate hemorrhages were noted in the right temporal lobe. In a third animal, rat 92 (fig. 8), which was unconscious for about one hour after receiving nine blows in close succession and died seven days later, extensive subarachnoid hemorrhages were seen in the temporoparietal region of both hemispheres, in the cerebellum and in the brain stem, with slight hemorrhagic involvement of the cerebral cortex. A fourth animal, rat 94 (fig. 8), made unconscious by fifteen blows in close succession, revealed at its death, four days later, a thin layer of clotted blood between the cerebellum and the meninges.

Hemorrhagic changes, of less extent, were seen in 3 other rats which had repeatedly been made unconscious by several blows delivered at intervals of two to six days (table 3). In 1 animal, rat 41 (fig. 9 *A*), the significant changes consisted of a subarachnoid hemorrhage encroaching on the olfactory lobes and the tips of the frontal lobes; in another, rat 38 (fig. 9 *C*), small hemorrhagic effusions were seen deeply embedded in the cerebellar white matter. In a third, rat 27 (fig. 9 *B*), several collections of recently extravasated red blood cells were seen in the cortex of the cerebral hemispheres.

Microscopic Observations.—The hemorrhages in these animals certainly constituted the most obvious evidence of lesion, but they did not indicate that the damage had been restricted to these areas; in fact, other parts, apparently undamaged, of the same injured brains, when examined with specific methods, showed evidence of more extensive organic damage, involving, in a disseminated fashion, both nerve cells and nerve fibers. This appeared to be true, also, for other animals, in which, unexpectedly, properly stained sections revealed damage the existence of which could hardly be suspected on gross inspection of the brains, and even on examination of the sections routinely stained with hematoxylin and eosin.

In the rats which had received the repeated blows in close succession the evidence of neuronal damage was found to be at the same stage in the different areas of the brain of the same animal (figs. 10, 11, 12 and 14). Progressive stages of a fundamentally similar neuronal injury were seen, on the contrary, in different areas of the same brain in the animals submitted to the trauma at longer intervals, suggesting cumulation of damage with each successive blow (fig. 13).

Of these changes of microscopic dimensions, the most apparent was rarefaction of the nerve cells of the cerebral cortex. This rarefaction was not diffuse, as areas showing normal stratification and density of nerve cells alternated with other areas exhibiting obscuring of stratification and diminution of neurons, affecting especially the pyramidal cells. Elsewhere the nerve cells seemed to be undergoing some form of gradual atrophy, with shrinkage of the cell bodies, which stained deeply and showed absence of expansions (aneuritic cells). Other cells exhibited diminished clearness of the cell outlines, with tigrolysis, or glassy cytoplasm, or with huge cytoplasmic vacuoles, which displaced the nucleus to the periphery of the cell body. Around these damaged elements groups of glia cells were noticeable at times.

With corresponding distribution, the apical dendrites appeared thickened, with a somewhat spiral course and at times a definite corkscrew shape. Some of these apical dendrites were poorly impregnated; others were overstained with the reduced silver. Pale and deeply stained segments often alternated in the same fiber. More advanced neurolytic changes were noticeable in other areas of the same brains, in which the situation of the apical dendrites was indicated by only a few fragments and by tail-like rows of disappearing granules. The focal distribution of these changes resulted in an irregular alternation in the same microscopic field of apical dendrites apparently intact and of other dendrites revealing all stages of a progressive neurolytic process.

The same type of focal change was shown by the medullated axons, which in scattered areas displayed varicose swelling and corkscrew twisting, with formation of peculiar loops and spirals. Other fibers revealed evidence of fragmentation, with dustlike granules and balls here and there, mostly free but occasionally still hanging to the ends of the degenerated portions of interrupted fibers.

Changes of corresponding severity were displayed by the myelin sheaths, some of which showed fusiform or ovoid swelling, resulting in a moniliform appearance, which contrasted sharply with the straight linear course of nearby undamaged sheaths; other sheaths appeared to be under incipient reabsorption, with resolution into round, oval or irregularly shaped globules. Disseminated areas of complete demyelination were occasionally seen; and where demyelination and breaking down of axons were still continuing, there was a quantitative increase of microglia cells, with all stages of transformation into rod cells, various bizarre-shaped scavenger cells and,

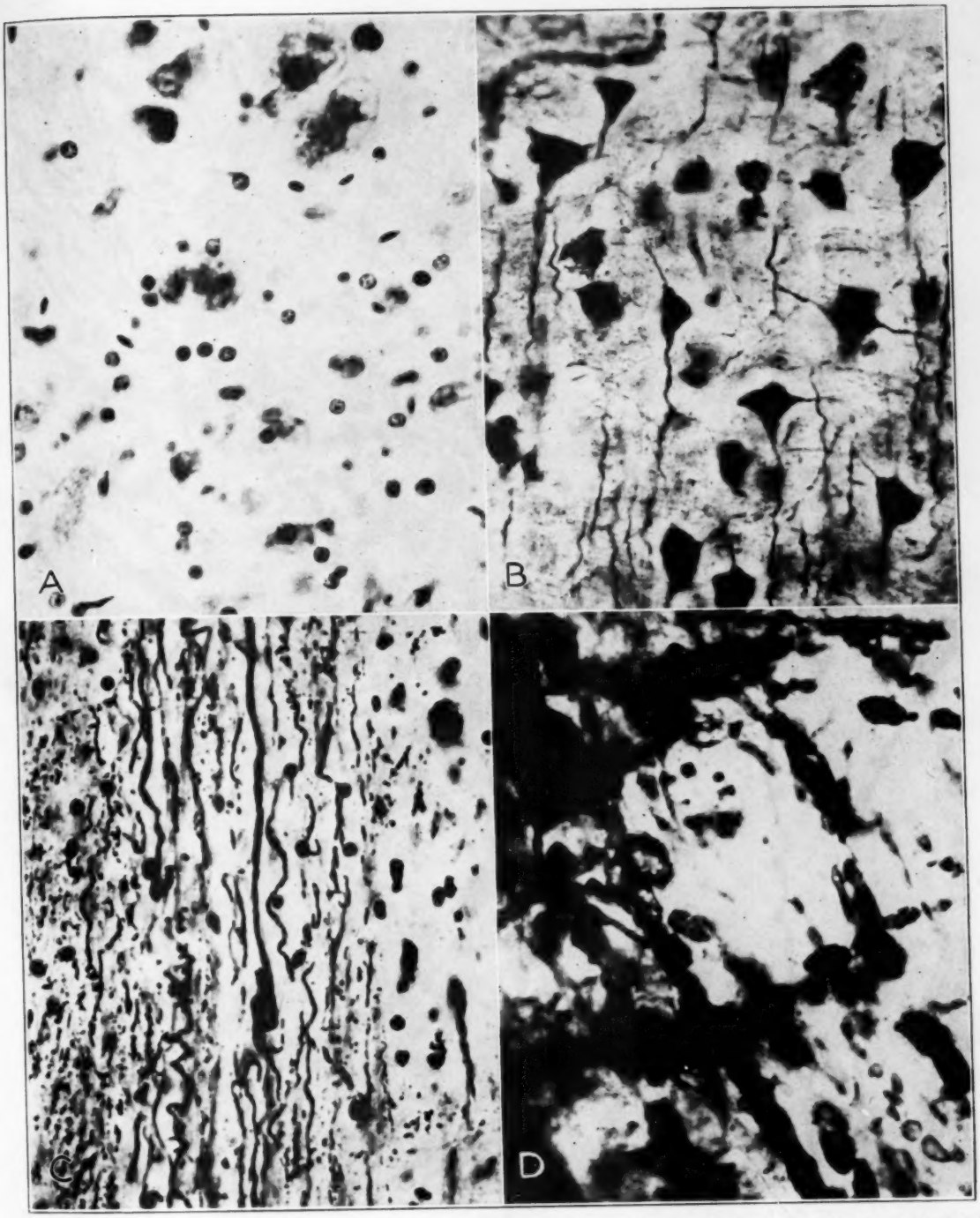

Fig. 10.—*A*, swelling, vacuolation and pericellular edema of nerve cells in the cortex of the frontal lobes of rat 99, which was unconscious for five minutes after receiving eleven subconcussive blows in close succession (moving head struck against stationary object). Three hours later, when the animal was killed, the skull, brain and cerebral involucres were apparently intact. Nissl stain; ocular 6; objective 40.

B, from a section at the same level as that from which *A* was taken, showing thickening, spiroid course and, at times, corkscrew twisting of the apical dendrites. Cajal stain; ocular 6; objective 40.

C, bundle of medullated axons in the right frontothalamic tract of rat 99, showing swelling, twisting, spiroid course and fragmentation of nerve fibers and overstaining nerve fibers with the reduced silver (preservation necrosis). Cajal stain; ocular 4; objective 40.

D, individual myelin sheaths from a section at the same level as that from which *C* was taken, showing moniliform swelling and fragmentation, with reabsorption in areas and resolution into round, oval or irregularly shaped globules. Spielmeyer stain; ocular 6; objective 40.

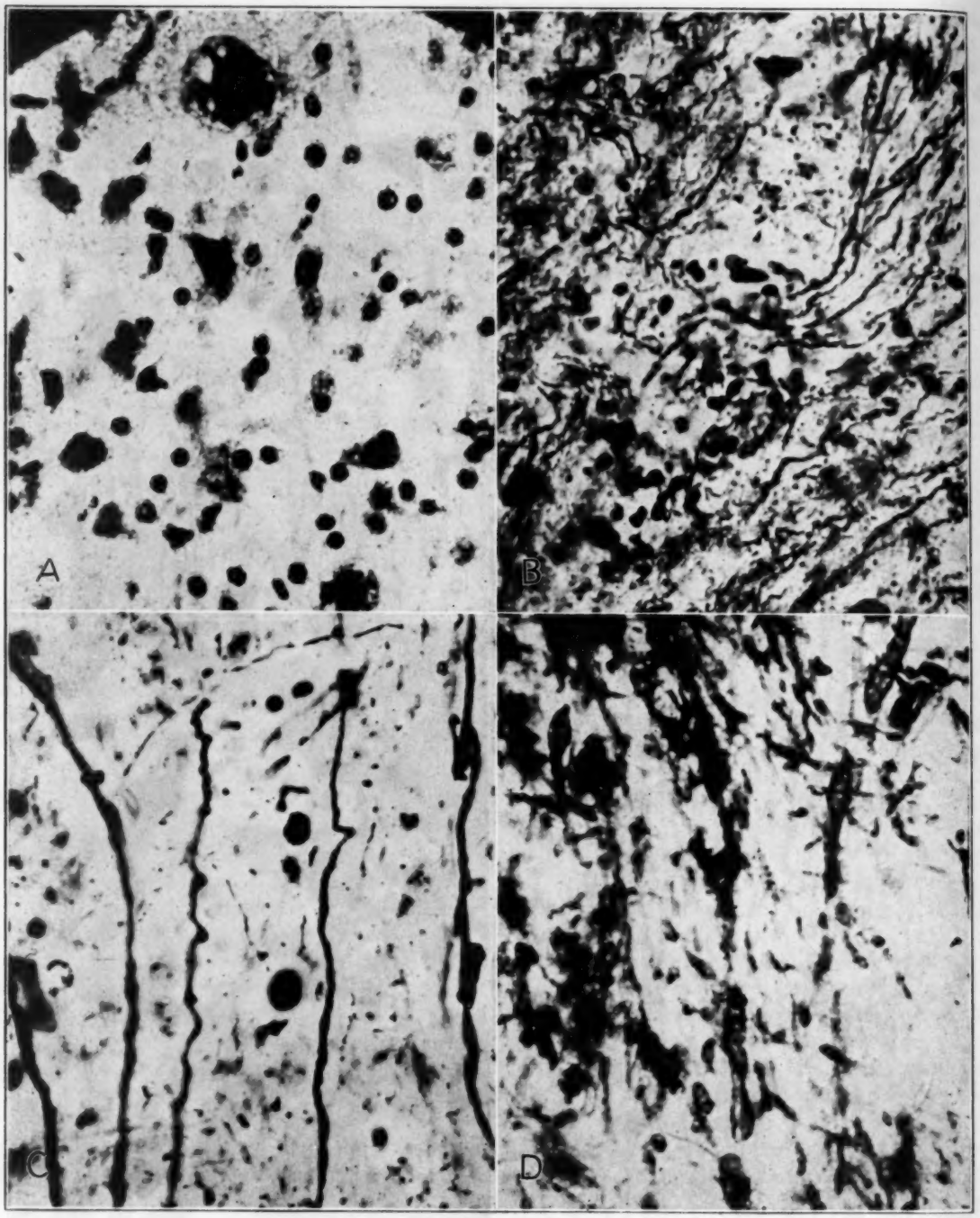

Fig. 11.—*A*, from the brain of rat 75, which received the same treatment as rat 99, eleven subconcussive blows in close succession, but with the other mechanism of trauma—moving object striking against the stationary head. At the last blow the animal was unconscious for four minutes, and it was killed three hours later. The Nissl preparation showed tigrolysis and pronounced pericellular edema of cortical nerve cells. Ocular 6; objective 40.

B, a bundle of medullated axons in the floor of the fourth ventricle of rat 75, displaying nerve fibers which are spread apart, fragmented and undergoing incipient granular disintegration. Evidence of mobilization of microglia cells is already noticeable in the damaged area. Ocular 6; objective 10.

C, from the field shown in *B*, higher magnification, showing the marked twisting and spreading apart of nerve fibers, with formation of bizarre-shaped loops and spirals. Cajal stain; ocular 6; objective 40.

D, myelin preparation of a section at a corresponding level, showing conspicuous varicose swelling and disintegration of myelin sheaths, with formation of ellipsoids and fat droplets. Spielmeyer stain; ocular 6; objective 40.

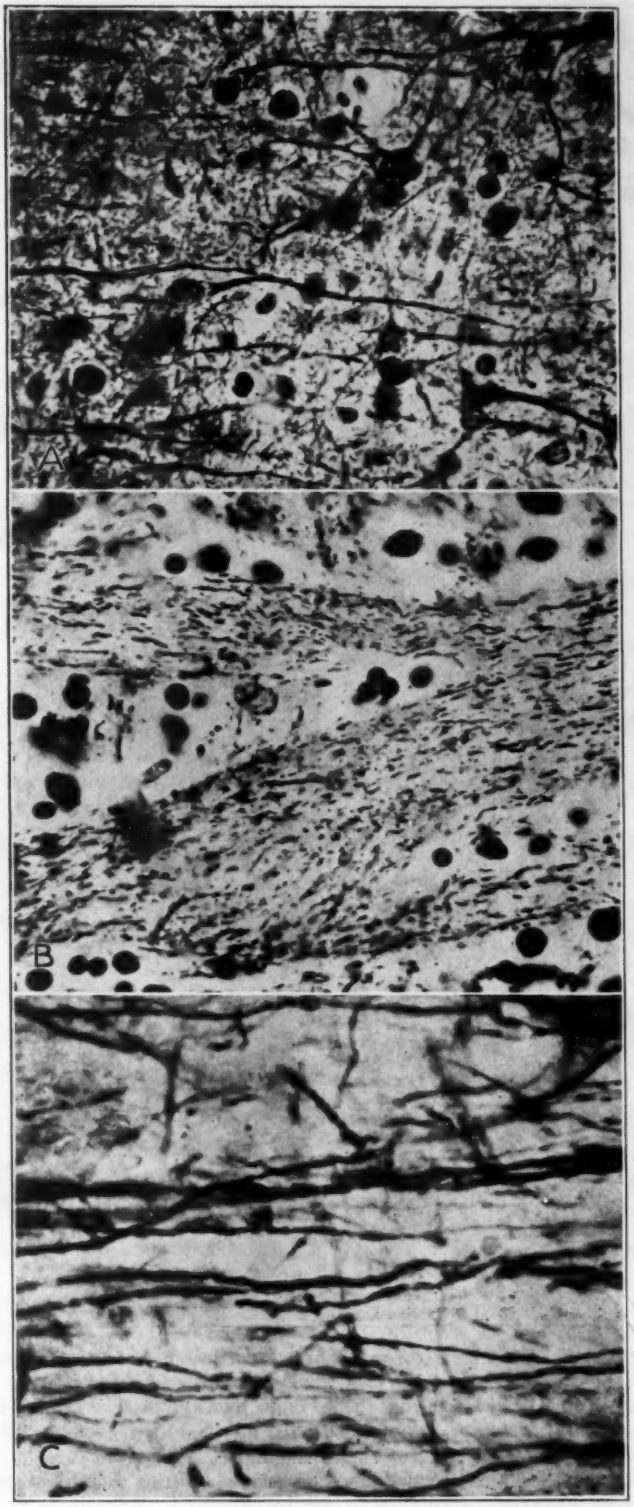

Fig. 12.—From the brain of an animal, rat 101, apparently unaffected by trauma of a severity approximately corresponding to that received by rats 99 and 75—fifteen blows in close succession, with the moving head struck against a stationary object. The rat was killed three hours later. The straight and regular course of the axis-cylinders (*A*, Cajal stain); the compactness of the bundles of nerve fibers, which appear to be homogeneously stained (*B*, Cajal stain), and the linear arrangement and uniform thickening of the myelin sheaths (*C*, Spielmeyer stain) are in sharp contrast to the corresponding damaged structures of rats 99 and 75. Ocular 4; objective 40.

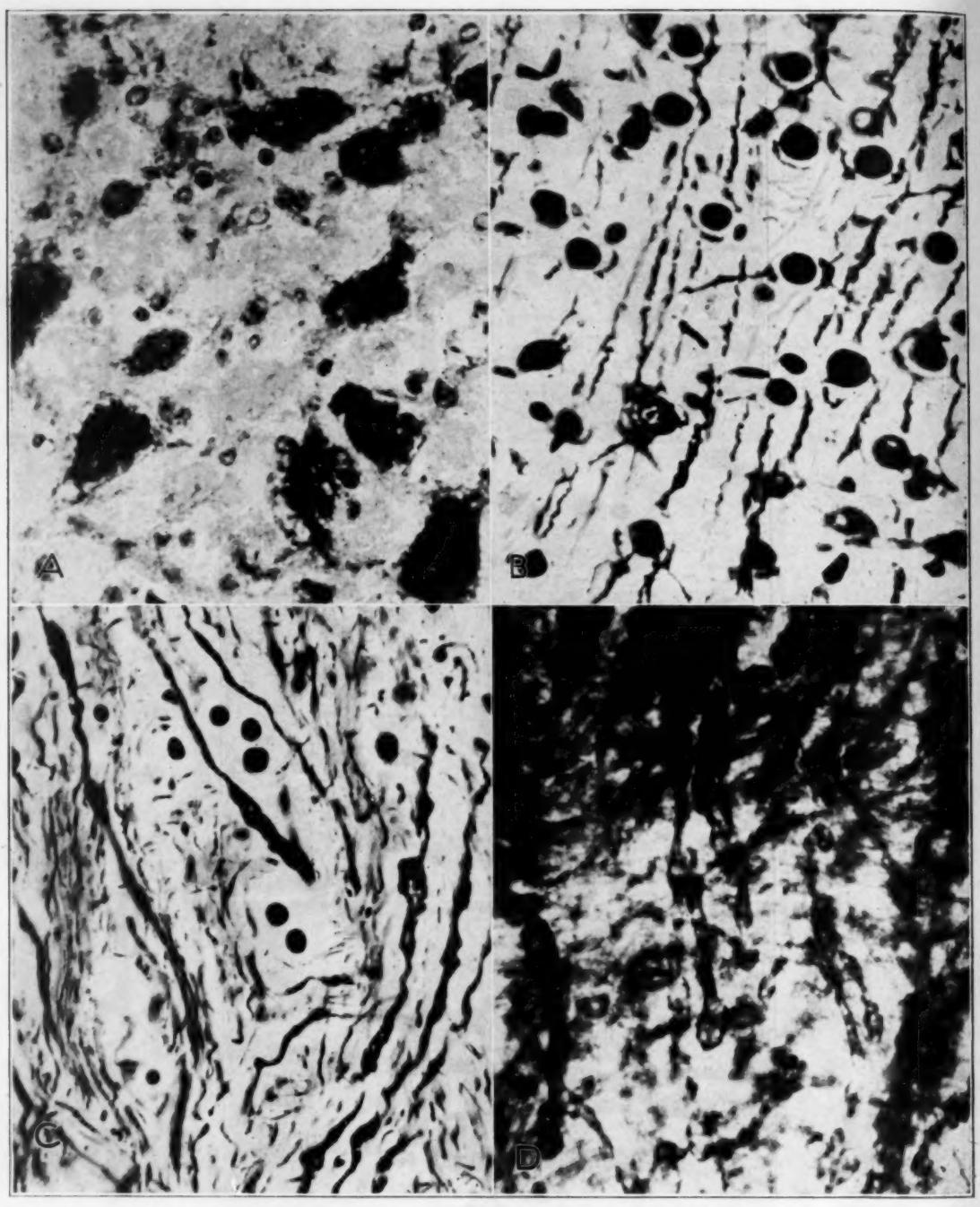

Fig. 13.—*A*, tigrolysis, swelling and pericellular edema of cortical nerve cells, from the brain of an animal, rat 35, which received eight subconcussive blows at long intervals—with the moving head struck against the stationary object—and was made unconscious at the seventh and eighth blows. At death, twenty-four hours later, the skull, brain and cerebral involucres were apparently intact. Nissl stain; ocular 6; objective 40.

B, from a Cajal preparation taken at a level corresponding to that from which *A* was taken, showing absence of expansions of the nerve cells (aneuritic cells), corkscrew twisting and fragmentation of the axons and tail-like rows of disappearing granules. Ocular 6; objective 40.

C, from a section at the level of the pons of rat 35, showing twisting and fragmentation of fibers, with formation of bizarre-shaped loops and spirals. The fusiform swelling at the ends of the degenerated portions of the interrupted fibers is clearly seen. Cajal stain; ocular 6; objective 40.

D, myelin swelling at the ends of the degenerated portions of fragmented fibers, from a section obtained at a level corresponding to that from which *C* was taken and stained for myelin by the Spielmeyer method. Ocular 4; objective 40.

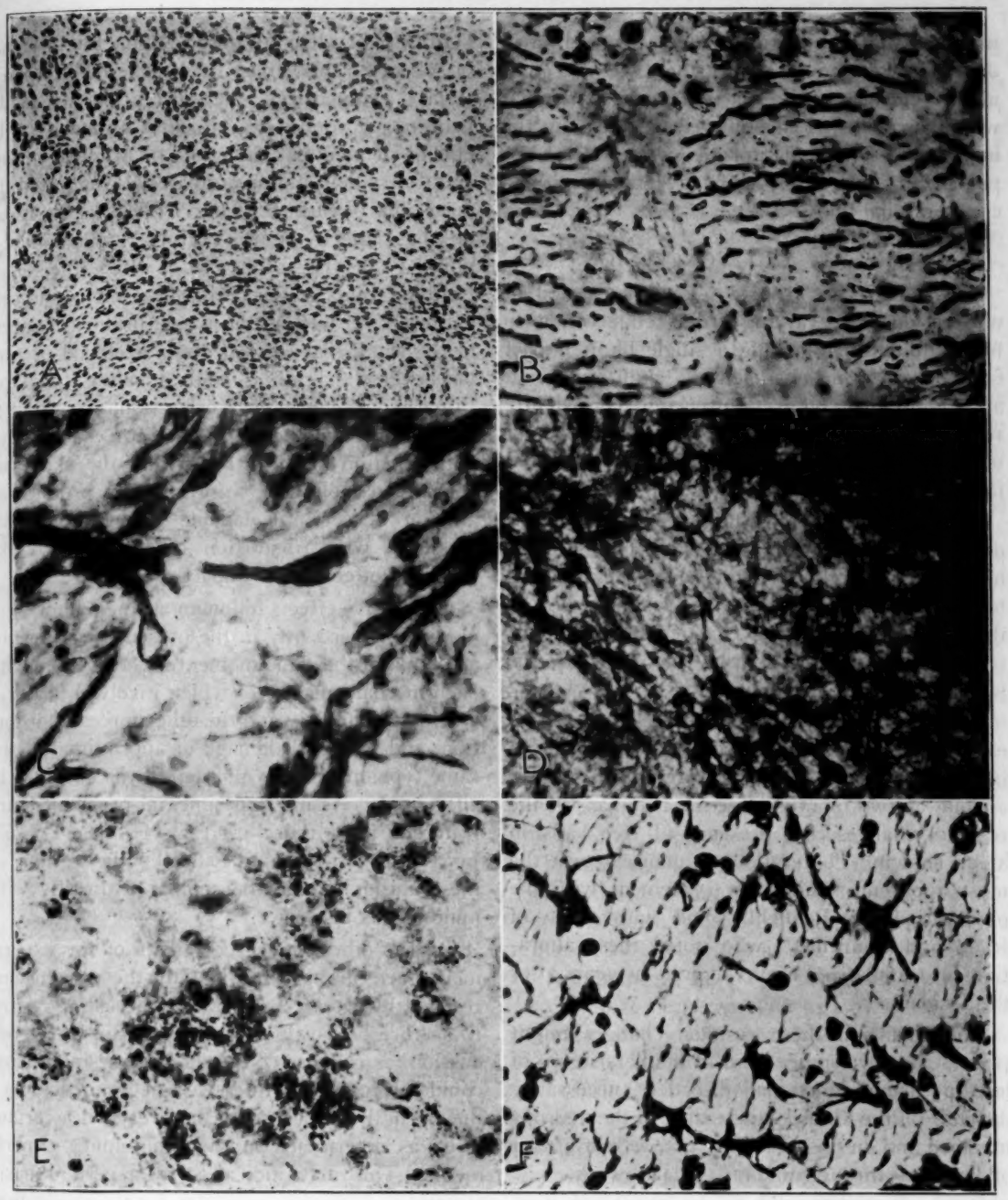

Fig. 14 (rat 54).—*A*, obscuring of stratification, shrinkage and pyknosis of nerve cells of the cortex (occipital lobe) in a rat which after the trauma had shown marked psychomotor disorders (figs. 5 and 6). The animal was unconscious for a few seconds after receiving fourteen subconcussive blows in close succession on the stationary head and died twenty-nine days later. The skull, brain and meninges did not reveal any abnormalities post mortem. Nissl stain; ocular 4; objective 10.

B, remnants of medullated axons, showing fusiform swelling and typical bulbs of retraction at the ends of degenerated portions of fragmented fibers. Cajal stain; ocular 6; objective 10.

C, myelin swelling, resulting in clublike formations at the ends of fragmented fibers, from a section taken at a level corresponding to that of *B*. Spielmeyer stain; ocular 6; objective 40.

D, from another area of the brain of the same rat, showing extensive reabsorption of myelin and resolution into round, oval or irregularly shaped globules. Spielmeyer stain; ocular 4; objective 40.

E, fat globules, for the most part free and to a less extent contained within compound granular corpuscles in a preparation taken at approximately the same level as that shown in *C* and stained with oil red O. Ocular 4; objective 40.

F, hyperplasia of astrocytes, not accompanied with any appreciable increase of glia fibers, in a damaged area of the perithalamic region of the brain of the same rat. At the center of the picture a ball-like formation hanging at the end of a fragment of nerve fiber is recognizable. Cajal stain; ocular 6; objective 40.

ultimately, into round, vacuolated cells, with small dark nuclei and cytoplasm loaded with fat globules. Evidence of glia reaction in the parts that were damaged was encountered at times, but the hyperplasia of the astrocytes was not accompanied, in most cases, with any appreciable increase of glial fibers.

COMMENT AND CONCLUSIONS

Rats recovering from a temporary period of unconsciousness, varying from ten seconds to fifteen minutes, following a single blunt impact on the head which had left the skull and brain apparently intact on gross inspection, consistently revealed widespread microscopic evidence of neuronal injury, affecting in a disseminated fashion both nerve cells and nerve fibers.

These findings suggest that concussion may be due to neuronal injury detectable with present histologic methods. Nothing more definite can be claimed, however, since one cannot rule out the possibility that these changes are secondary to other factors primarily involved in the phenomenon of concussion.

Evidence of neuronal damage was noticed as early as one to two hours after the trauma, and in a few animals the lesions were seen to persist as long as two months after the trauma. Of the residual changes, the presence of free balls in areas showing obliteration of neurons was the most apparent. This is in agreement with the observations of Penfield,[18] and with those of Rand and Courville,[10] who noted these alterations in traumatized brains months or years after the accident.

The part that these residual changes might play in the development and in the persistence of late-appearing functional disorders necessarily depends on the location and extent of the neurons involved and on the possibility of a redistribution of impulses through undamaged pathways.

In an attempt to analyze the possible factors which could account for these neuronal changes, it becomes apparent that nerve cells and nerve fibers may be affected in a number of ways after mechanical violence to the head. Cerebral edema, cortical and subcortical hemorrhage, so much emphasized by other investigators in interpreting changes in neurons, not only in contused areas but in remote and otherwise undamaged portions of the brain (Greenfield,[14] Schwartz and Fink [13]), were rarely encountered in my material. In the light of old and recent observations, the influence of "shear strains" must be considered. Ramón y Cajal [19] emphasized the susceptibility of the neurons of young experimental animals to the effects of minimal amounts of trauma. Rand and Courville,[10] in human material, suggested the possibility of rupture of nerve fibers as the result of the "shock of the injury." Greenfield [14] pointed out the facility with which the single anatomic units of the brain and their connecting pathways, as well as the whole brain in relation to the skull, may be distorted, stretched or torn whenever the brain is made to alter its shape. Forces connected with acceleration, according to Denny-Brown and Russell,[4] and forces connected with rotation of the brain within the skull, according to Holbourn,[20] are likely to produce an amount of cerebral damage greater than that produced when distortion of the skull is the principal effect of the impact.

Concussive effects following a single blow were obtained consistently in the present experiments, a trauma of the same momentum being used with each mechanism, one of which involved forces of acceleration mainly and the other forces of distortion, and neuronal damage of approximately the same type, magnitude and depth was observed in all animals. As my experimental procedures are different from those used by Holbourn [20] and by Denny-Brown and Russell,[4] the results of these authors cannot be compared directly with mine in this respect.

On the other hand, the results of my experiments are in agreement with the conclusions reached by Denny-Brown and Russell in regard to a "threshold value" in the mechanism of concussion, as concussive effects after a single blow could be obtained with consistent frequency once the strength of the trauma had reached a certain level, as determined in the preliminary experiments. This may indicate that a certain basic amount of damage is necessary for the production of the phenomenon of concussion.

If this concept is true, the appearance of ill effects as a result of repeated trauma of minimal intensity might be explained on the basis of cumulated neuronal damage, until the "threshold value" is reached and functional disorders become apparent. Evidence in support of this concept was clearly found in my material, as rats

18. Penfield, W.: Cerebral Cortex in Man: Cerebral Cortex and Consciousness (Harvey Lecture), Arch. Neurol. & Psychiat. **40**:417 (Sept.) 1938.

19. Ramón y Cajal, S.: Degeneration and Regeneration of the Nervous System, translated by R. M. May, London, Oxford University Press, 1928, vol. 2.

20. Holbourn, A. H. S.: Mechanics of Head Injuries, Lancet **2**:438 (Oct. 9) 1943.

submitted to repeated blunt impacts on the head the strength of each of which alone was not sufficient to harm the animal, after a certain number of blows began to reveal ill effects, as shown by unconsciousness, with or without recovery, and at times by persisting functional disorders or by delayed death.

When the repeated subconcussive blows were delivered in a short period, there was a somewhat higher incidence of ill effects than when the trauma was delivered at longer intervals. An explanation of this might be found in the recovery of reversible lesions and in the redistribution of impulses through undamaged nerve pathways in the longer intervals between the blows.

In the great majority of animals there was a certain correspondence between the response to the repeated trauma during life and the amount and extent of cerebral damage, as the latter appeared to be minimal in the animals clinically unaffected and became progressively more severe in the animals which were made repeatedly unconscious or manifested persisting functional disorders as the result of the repeated trauma. In these animals, also, no remarkable differences were noticed in the apparent effects under the two mechanisms of trauma.

Among the postmortem changes, punctate hemorrhages or other types of hemorrhagic change were extremely rare in this material. I am unable therefore to confirm the observation of Shaller, Tamaki and Newman [3] of an apparent increase in vulnerability of the cerebral vessels induced by the application of repeated blows. Evidence of neurolytic changes, accompanied by loss of myelin and, in the later stages, by glial proliferation, was, on the contrary, consistently encountered in my animals.

Assuming that the normal function of the brain is dependent on two factors—the initiation of impulses within the nerve cells and their transmission through the complicated network of nerve fibers—my results point strongly to the possibility of permanent functional disorders, such as those seen in some of the animals, following repeated blows on the head apparently of moderate intensity, the disorders being due not only to a deleterious effect on the nerve cells but to the interruption of nerve impulses consequent to the changes in the nerve fibers.

SUMMARY

Rats submitted to repeated blunt impacts on the head the strength of each of which alone was not sufficient to harm the animal (subconcussive trauma) began to reveal ill effects after a certain number of blows, as shown by unconsciousness, with or without recovery, at times by other, persisting functional disorders and later even by death. When the repeated subconcussive blows were delivered in a short period—one impact after another, one minute apart—there was a somewhat higher incidence of ill effects than when the trauma was delivered at longer intervals—from two to six days apart. No remarkable differences were noticed in the effects when, with a trauma of the same strength, the head in rapidly accelerated motion was made to strike a stationary object and when a moving object was made to strike the fixed head of the animal. In the great majority of animals there was a certain correspondence between the response to the repeated trauma during life and the amount and extent of cerebral damage. Among the postmortem changes, hemorrhage or any other type of change detectable on gross inspection was extremely rare. On the contrary, widespread evidence of neuronal injury, affecting in a disseminated fashion both nerve cells and nerve fibers, accompanied with loss of myelin and, in the later stages, with glial proliferation, was a consistent microscopic observation.

A neuronal injury identical in type was found in collateral experiments in animals recovering from a temporary period of unconsciousness following a single blow on the head which had left the skull and brain grossly intact. Microscopic evidence of neuronal damage was noticed in these animals as early as one to two hours after the trauma, and in a few instances the lesions were seen to persist as late as two months after the trauma. These observations suggest that concussion may be due to neuronal injury detectable with the present histologic methods. With the production of concussion by a single blow, no pronounced differences were noted in the effects when the impact was delivered on the stationary head and when it was delivered on the head in rapidly accelerated motion, with a trauma of the same momentum.

NOTE: This paper was already in course of publication when two important experimental studies on head trauma came to my attention.

In one, by Gurdjian and Webster,[21] it is concluded:

> Higher velocities were required to produce [in dogs] pathophysiologic effects under the circumstances of the

21. Gurdjian, E. S., and Webster, J. E.: Experimental Head Injury with Special Reference to the Mechanical Factors in Acute Trauma, Surg., Gynec. & Obst. **76**:623 (May) 1943.

nonfixed head than the fixed head. . . . However, a greater degree of mass movements of the brain may occur under conditions of a nonfixed head.

In the other, Windle, Groat and Fox [22] found definite neurologic changes accompanied by a variable amount of swelling of the sheaths of the nerve fibers in guinea pigs struck on the head once or repeatedly. In agreement with my own observations, the amount of damage they found was proportionate to the strength and number of blows; and in a limited number of animals, while a single subconcussive blow was ineffective, two subconcussive blows produced as much damage as a single light concussive blow. Hence their conclusion that "these histological changes do serve as visible indicators of the ravages of a concussional force."

Medfield State Hospital.

22. Windle, W. F.; Groat, R. A., and Fox, C. A.: Experimental Structural Alterations in the Brain During and After Concussion, Surg., Gynec. & Obst. **79**:561 (Dec.) 1944.

STUDIES OF THE SENSATION OF VIBRATION

III. EVIDENCE FOR CORTICAL AREAS IN INHIBITION AND MEDIATION OF TICKLE

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CHICAGO

In experiments on the functions of the frontal lobe, we performed a number of different examinations,[1] among which was the determination of the vibratory threshold. Of 3 patients with lesions of the right frontal lobe who were examined, the results for 1 lead us to conclude that two areas are present in the cortex in the mediation of tickle: One area is the primary tickle center, and the other area inhibits this center. This peculiarity of the functions of the cortical areas involved in the perception of tickle, and the belief that tickle is not a pure sensation but is produced by a combination of sensory qualities, such as touch and pain,[2] with the consequent rare examination of the patient with neurologic lesions for tickle, largely account for the fact that the areas for tickle have not been discovered before.

REPORT OF A CASE

An American-born woman, predominantly right handed, was operated on twice for a tumor of the right frontal lobe. On Jan. 18, 1940, at the age of 37, she was first admitted to the hospital, with a history of convulsions, dizziness, vomiting, diminution of vision and slowing of mental processes. These symptoms had increased in severity for six months preceding her admission to the hospital. Examination showed bilateral loss of vision and slight paresis of the muscles of the left side of the face, the right palpebral fissure being wider than the left. A ventriculogram confirmed the diagnosis of tumor of the right frontal lobe. Operation was performed on January 24, and a cystic tumor (later determined to be a protoplasmic astrocytoma) was removed. The mass of tissue extirpated weighed 106 Gm. The area of the tissue removed in this patient (*6*) is shown diagrammatically in figure 1. This figure also shows the areas of the extirpated tissue in 2 other patients (*1* and *4*) with lesions of the right frontal lobe whose vibratory thresholds were determined, and a diagram indicating the overlapping of the areas of the lesions of the last 2 patients with the area of extirpation in the first patient.

The patient's recovery was uneventful, and no neurologic dysfunction was present except the loss of vision. She was able to perceive bright lights and movement but could not perceive any details. Her postoperative intelligence quotient for the verbal part of the Wechsler-Bellevue test was 116. She began to study Braille and made other adequate adjustments to her environment. The only personality characteristics which could be associated with the lesion was a mild degree of facetiousness and irritability.

Twenty months after the operation a relapse occurred. The patient had numerous convulsions, involving largely the left side of the face and the left arm, and headaches in the area of the right temporal lobe. A second operation was performed on Dec. 12, 1941, at which time 90 Gm. of tissue was removed. A photograph of the area of the lesion produced by the two operations is shown in figure 2. The postoperative recovery of the patient was at first uneventful. The neurologic symptoms consisted of some motor paralysis, decrease in the sensation of touch and astereognosis involving in each case the left side of the body. On Jan. 26, 1942 the patient became mentally confused. Rage reactions occurred periodically. She had visual hallucinations and became incoherent and extremely facetious. These periods were interspersed with periods of lucid behavior and lethargy. On March 20, 1942 she died, of circulatory failure with pneumonia and encephalitis.

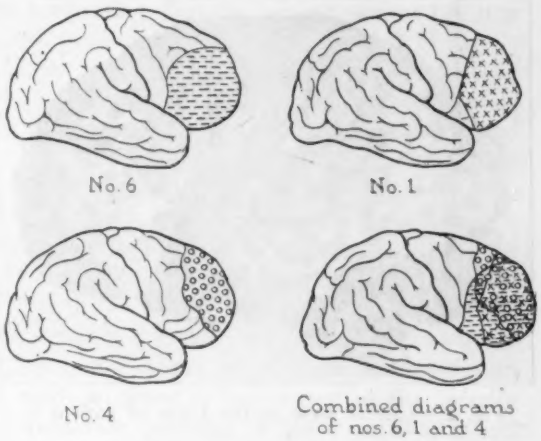

Fig. 1.—Diagrams showing the amount of tissue extirpated after the first operation on patient 6, who displayed the abnormal tickle response, and the lesions of 2 control patients, 1 and 4. The composite diagram shows that the lesions of the controls did not overlap the lesion of patient 6 in the inferior and posterior areas.

From the Department of Nervous and Mental Diseases and the Department of Surgery, Northwestern University Medical School.

1. Yacorzynski, G. K., and Davis, L.: Modification of Perceptual Responses in Patients with Unilateral Lesions of the Frontal Lobes, Tr. Am. Neurol. A. **68**: 122, 1942; An Experimental Study of the Functions of the Frontal Lobes in Man, Psychosom. Med. **7**:97, 1945.

2. Since, to the best evidence, tickle is not a simple sensation but is produced by a combination of sensory qualities, it is only logical that this response be classified as a perception rather than a sensation.

DETERMINATION OF VIBRATORY THRESHOLDS

The vibratory thresholds were determined by an apparatus which has already been described [3] and which allows measurement of the thresholds through a large range of sinusoidal frequencies, with precise determination of the amplitude of the vibrating pointer when placed directly against the skin. After the first operation attempts were made to measure the vibratory thresholds of the patient at the different frequencies, with the result that, rather than experiencing the sensation of vibration, she usually perceived tickle, which was at times so excruciating that she would break out into hilarious laughter. The finger tips, the ventral and dorsal surfaces of the hands and arms and the sides of the face were examined. The sensation of tickle was more pronounced on the left side of the body than on the right side. Thus, on the ventral surface of the left hand she perceived a sensation of tickle at all of the frequencies which could be tested with the apparatus (from 50 to 500 double vibrations), whereas on the right side she perceived the vibrations at all of the frequencies except at 50 double vibrations, at which she perceived tickle. Intermittently, on the areas of the right side which were tested she would at times fail to perceive tickle at some frequencies,

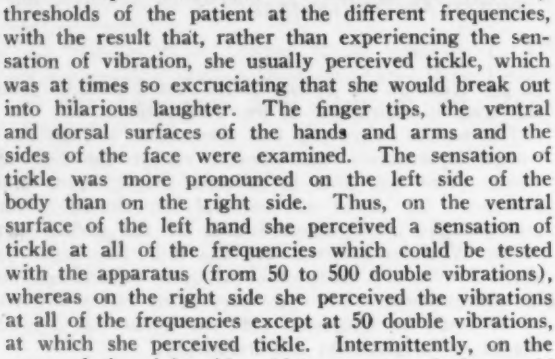

Fig. 2.—Lateral view of the brain of patient 6.

although this occurred very seldom when the left side was stimulated. She reported that she had become more ticklish after the operation but that prior to the operation she had not considered herself abnormally ticklish. To substantiate this statement, she recounted the following incidents: While at the hospital after the first operation the nurse was greatly annoyed by her laughter when she was given a bath and a massage. The patient stated, "I felt as if the nurse was hitting every ticklish spot I had." When she returned home, her sister discovered that all she had to do to win an argument was to tickle the patient.

These results were unusual in that normal subjects studied by us seldom report a sensation of tickle when the vibrating pointer is placed against the skin, and that 2 other patients with cerebral lesions of the right frontal lobe experienced only the normal vibrations and gave threshold readings characteristic of normal subjects. Being cognizant, however, that there is a wide difference between persons in susceptibility to tickle, and that tickle is subject to much learning, we did not place great emphasis on the results until the second operation. At that time the perception of tickle to the vibratory stimulus disappeared completely on both sides of the body, and, although the patient was examined a number of times, no tickle response to the vibratory stimulus could be elicited. The patient also reported that she was no longer ticklish.

INTERPRETATION

These results can be interpreted by postulating that an area exists in the brain which is involved in the mediation of the perception of tickle and that a second area is present which inhibits the primary tickle area. When the inhibitory area is destroyed, a release of the inhibition takes place, so that tickle becomes more pronounced. Presumably, that is what occurred after the first operation. The second operation, according to this conception, would have destroyed the primary tickle area.

In advancing the conception that an area is present in the cortex which functions to inhibit another cortical area, we are not postulating a completely novel mechanism. Dusser de Barenne, Garol and McCulloch,[4] Fulton and Kennard [5] and Hines [6] have shown that areas are present in the frontal lobes which function to inhibit the motor cortex. Two areas, 4 S and 8 S, which inhibit area 4 have been identified in the monkey. The release phenomenon of the tickle reaction simulates the release of the motor responses in other ways. We found that although tickle was obtained predominantly when the contralateral side of the body was stimulated, the response in general had a bilateral distribution and showed no evidence of topographic localization. Hines [6] has shown that removal of the "strip" area (area 4 S) on one side produced a generalized bilateral motor release, although contralateral symptoms were dominant.

The area involved in the inhibition of tickle can be estimated by comparing the size of the lesion of the patient who displayed the release phenomenon with the amount of destruction of 2 other patients with lesions of the right frontal

3. Yacorzynski, G. K., and Brown, M.: Studies of the Sensation of Vibration: I. Variability of the Vibratory Threshold as a Function of Amplitude and Frequency of Mechanical Vibration, J. Exper. Psychol. **28**:509, 1941. Brown, M., and Yacorzynski, G. K.: Studies of the Sensation of Vibration: II. Vibration Sensibility in the Face Following Retrogasserian Neurectomy, Arch. Neurol. & Psychiat. **47**:813 (May) 1942.

4. Dusser de Barenne, J. G.; Garol, H. W., and McCulloch, W. S.: Physiological Neuronography of the Cortico-Striatal Connections, A. Research Nerv. & Ment. Dis., Proc. **21**:246, 1942.

5. Fulton, J. F., and Kennard, M. A.: Study of Flaccid and Spastic Paralyses Produced by Lesions of the Cerebral Cortex in Primates, A. Research Nerv. & Ment. Dis., Proc. **13**:158, 1934.

6. Hines, M.: The "Motor" Cortex, Bull. Johns Hopkins Hosp. **60**:313, 1937.

lobes who did not show an abnormal change in perception of tickle. A diagram showing such a comparison is included in figure 1. It is seen that the lesions of the controls do not overlap the lesions of the patient showing the release of tickle in Brodmann's areas 44 and 45, the dorsal parts of areas 11 and 47 and the lower anterior part of area 9. Presumably, therefore, the center inhibiting tickle is located in these areas.

The determination of the center involved in the mediation of tickle presents more difficulty, since any part of the cerebrum destroyed by the second operation may be the area concerned. This lesion includes the Brodmann areas 41, 42, 43 and 52, the lower part of area 6, the lower tip of area 3, the anterior and inferior parts of area 40 and the superior portion of area 22. If tickle involves a perceptual response rather than a pure sensation, as the evidence on this sense seems to indicate, one would expect that its center would not be found in the postcentral gyrus involved in the mediation of the primary sensations, but would probably be posterior to this area, as is, for example, the case with stereognosis. This would involve the region which was destroyed on the inferior aspect of the parietal lobe, or area 40. We should not exclude, however, the possibility that involvement of the basal ganglia of the telencephalon following the second operation may have been responsible for the diminution of tickle, since a coronal section at the tips of the temporal lobes showed some traumatic and degenerated changes in these areas. Bucy [7] stated the opinion that areas 4 S and 8 S mediate the inhibitory impulses to the motor cortex through the basal ganglia. However, even should the impulses of the inhibitory tickle area reach the primary tickle area through neural connections with the basal ganglia, there is little reason to suppose that the interruption of such pathways would in any way produce a diminution of the release phenomenon following the destruction of the inhibitory center, unless, of course, the mechanism involved in the perception of tickle is entirely different from that existing in the motor field.

7. Bucy, P. C.: The Neural Mechanisms of Athetosis and Tremor, J. Neuropath. & Exper. Neurol. **1**: 224, 1942.

SUMMARY

Two operations were performed on the right cerebral hemisphere of a patient. After the first operation a vibrating pointer placed against various parts of the body elicited an intense perception of tickle. The hyperesthesia showed no topographic localization and was bilateral, although it was more pronounced when the contralateral side of the body was stimulated. After the second operation the response of tickle to a vibrating stimulus disappeared. In normal subjects and in 2 subjects with lesions of the right frontal lobe a vibrating stimulus applied against the skin seldom produced a sensation of tickle.

These results indicate that in the mediation of tickle two centers are involved. One center is primarily involved in the mediation of tickle, and the other inhibits the tickle center. According to this conception, the inhibitory center was destroyed after the first operation, producing the release phenomenon, and the tickle center was destroyed after the second operation, eliminating the abnormal tickle response. A mechanism similar to the one described here has been found for the motor responses. The inhibitory center for tickle appears to be located in the inferior and posterior portions of the frontal lobe and the tickle center probably in the inferior part of the parietal lobe.

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PRETRAUMATIC PERSONALITY AND PSYCHIATRIC SEQUELAE OF HEAD INJURY

I. CATEGORICAL PRETRAUMATIC PERSONALITY STATUS CORRELATED WITH GENERAL PSYCHIATRIC REACTION TO HEAD INJURY BASED ON ANALYSIS OF TWO HUNDRED CASES

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Psychiatric symptoms are common among the sequelae of head injury.[1] These symptoms may vary in quantity, intensity and duration from case to case. At one extreme may be merely increased irritability. At the other extreme may be a fully developed neurotic syndrome. In association with these symptoms are often prolonged invalidism and delay in resumption of occupation, or, in military life, delay in return to active duty.[3]

Various opinions have been offered as to the causation of these post-traumatic psychiatric syndromes. The subject has been ably reviewed by Strauss and Savitzky[4] and by Schilder.[5] The belief was expressed that the psychiatric sequelae of head injury are due mainly to anatomic and physiologic changes in the brain,[6] that they result from an interest in gaining compensation,[7] that they are largely ascribable to pretraumatic abnormalities of the personality[8] and that there is high correlation with various associated factors, such as occupational, litigational and marital stresses.[9]

This paper is the report of an investigation into the possible relation between the over-all pretraumatic personality and the psychologic sequelae of head injury.

MATERIAL

This inquiry was undertaken as part of a comprehensive study of civilian head injury conducted at the Boston City Hospital from July 1942 to October 1944 by a group under the direction of Dr. Denny-Brown, consisting of neurologists, psychiatrists, a psychometrist, an electroencephalographer, a social worker and a resident physician who had been trained in neurology and psychiatry.

Two hundred subjects were selected for intensive study out of 430 patients who were initially studied on their admission to the hospital. These 200 patients were selected by exclusion of persons in the following categories: persons under 15 and over 55 years of age, vagrants, irresponsible alcoholic addicts, chronically unemployed persons and a few others on whom follow-up study was unobtainable. The groups comprised 125 males and 75 females. The occupational distribution was as follows: skilled or semiskilled workers, 48 per cent; domestics or housewives, 19 per cent; students, 10 per cent; civil employees (firemen, police officers), 6 per cent; unskilled laborers, 5 per cent; unclassified persons, 12 per cent. All patients had been followed until their symptoms had disappeared and they had returned to full employment or for a period of at least six months from the time of discharge from the hospital.

All patients had been admitted to the hospital promptly after injury. In general they had suffered "closed" head injuries. Only 6 patients had compound fractures. The patients varied in their neurologic and psychologic manifestations. The injury of 85 patients would in general neurologic practice be diagnosed as

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Part II (in preparation) deals with multiple, specific personality factors present both before and after head injury.

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The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the President and Fellows of Harvard College.

1. (*a*) Denny-Brown, D.: Disability Arising from Closed Head Injury, J. A. M. A. **127**:429-436 (Feb. 24) 1945. (*b*) Symonds, C. P., and Russell, W. R.: Accidental Head Injuries: Prognosis in Service Patients, Lancet **1**:7-10, 1943.

2. Footnote deleted.

3. Lewis, A., in Discussion of Differential Diagnosis and Treatment of Postcontusional States, Proc. Roy. Soc. Med. **35**:607-614, 1942.

4. Strauss, I., and Savitsky, N.: Head Injury: Neurologic and Psychiatric Aspects, Arch. Neurol. & Psychiat. **31**:893-955 (May) 1934.

5. Schilder, P.: Neuroses Following Head and Brain Injuries, in Brock, S.: Injuries of Skull, Brain and Spinal Cord, Baltimore, William Wood & Company, 1940.

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7. Schaller, W. F.: After-Effects of Head Injury, J. A. M. A. **113**:1779-1785 (Nov. 11) 1939.

8. (*a*) Symonds, C. P.: Mental Disorder Following Head Injury, Proc. Roy. Soc. Med. **30**:1081-1094, 1937. (*b*) Symonds and Russell.[1b] (*c*) Lewis.[3]

9. Adler, A.: Mental Symptoms Following Head Injury: A Statistical Analysis of Two Hundred Cases, Arch. Neurol. & Psychiat. **53**:34-43 (Jan.) 1945.

"concussion," the degree of severity depending on the length of coma. Twelve patients had no initial traumatic impairment of consciousness other than a momentary daze. In all, 34 had fractures of the skull. The cerebrospinal fluid of 46 patients was blood tinged. Thirty-two patients presented abnormal neurologic signs. In 14 patients focal injury to the brain was indicated by the presence of cranial nerve palsies, dysphagia and/or convulsive seizures. Twenty patients had no history of coma following injury; 92 were in coma or semicoma for less than ten minutes; 42, from ten to thirty minutes; 20, from thirty to sixty minutes; 17, from one to six hours; 4, from six to twenty-four hours, and 4 over twenty-four hours. Eighteen patients were not disoriented; 155 patients showed disorientation for variable periods, up to twelve hours; 4 patients, from twelve to twenty-four hours; 12 patients, from one to seven days, and 11 patients over a week.

METHOD

Evaluation of the pretraumatic personality of each patient was based on a history of the personality. In the present state of psychiatry there is no more dependable method of gaining insight into the nature of a personality than through a scrutiny of past performances and experiences in their special settings. No personality test, such as the Rorschach or the Minnesota test, can be depended on to give an evaluation of a patient's personality before injury to the head when the test is given after the injury. Thus, chief reliance was placed on the psychiatric history.

Uniformity of examination was attained by having each patient in the series of 200 examined not only by one of the two psychiatrists in the group but by all the other members of the project staff, including, in most cases, the other psychiatrist. There was general staff discussion of the psychiatric aspects of each patient's case. In addition, each psychiatrist followed a uniform scheme of examination. Not only was the history taken from the patient himself, but the data were checked and supplemented by interviews with relatives, friends, employers and others who might be able to provide information about the patient's behavior. Investigations by a social worker were of particular assistance. At subsequent interviews with the patient the data were rechecked.

As a result of such an investigation, each patient was given a categorical classification of his personality under one of the following headings:

Normal personality
Psychopathic personality
Neurotic personality
Personality variant
Normal personality except for general nervousness
Mental deficiency
Neurotic traits in childhood
Behavior problem (childhood and youth)
Psychotic behavior
Pretraumatic personality unknown

It is recognized that no categorical classification can do justice to the complexity of a personality and that widely dissimilar personalities may be found in the same diagnostic group. Nor do I argue in favor of the validity of such generalization; the study merely tests it. For purposes of statistical analysis it is necessary to reduce psychiatric data to a classification of commonly recurring categories, in the terminology of common usage. The classification chosen has been such as to be readily identifiable by others.

Final decision as to the particular category in which a patient should be placed presented various difficulties, especially with patients who showed admixtures of traits. As there are no pure personality types, strict demarcation of boundary zones between categories depended on the application of clinical judgment in line with rather strict definitions. Some patients presented such a preponderance of certain traits that classification was easy. This applied particularly to some of the "neurotic" patients and the "psychopathic personalities." To be rated as "normal" the patient had to be a robust personality. The chief difficulty arose in consideration of the well integrated persons who showed slight degrees of neurotic traits or some other personality bias, such as exceptional egocentricity, irritability or sensitivity. Quantitation was in the last analysis a matter of clinical estimate. Some of the "normal" patients manifested on some occasions slight evidences of neurotic difficulties, but such episodes were so brief and transient as to have no influence on the general pattern of the personality. Those patients who, while free of characteristic neurotic symptoms, were somewhat more tense were classified as "essentially normal except for general nervousness." Particular difficulty involved the category of "personality variant." This included patients with definite bias in the personality, including particularly such traits as exceptional egocentricity, irritability, sensitivity and moodiness, but who, nevertheless, maintained a fairly stable and harmonious position in society. Obviously, the differences between such persons and "psychopaths" would be quantitative as well as qualitative. Exceptional sensitivity might well approach a paranoid level and indicate a categorical diagnosis of the schizoid type of psychopathic personality. Moodiness and emotionality might be so severe as to color the patient's relation to society and indicate a diagnosis of affective type of psychopathic personality. The diagnosis "personality variant," then, was based on the selection of patients who had such bias in the personality as to exclude them from the strictly "normal" group but who were not characteristically neurotic or psychopathic and whose bias was not that of simple general nervousness.

The main outlines of the categories which are presented here are offered in the following definitions:

Normal Personality.—A person who is in harmony with himself and his environment, is virtually free of psychoneurotic traits and other personality imbalances, is not habitually in conflict with the ethical and social standards of society, is free of addiction to alcohol, maintains satisfactory personal, social and occupational adjustments and presents a general integration of objectives and behavior. This does not exclude the possible existence of some personality bias, such as egocentricity or timidity, or even a history of brief or transient neurotic symptoms.

Psychopathic Personality.—A person who has shown extreme failure in social and intrapersonal adaptation, associated with impulsiveness, defective self control, lack of fixity of purpose, instability of effort and undependability in his work. In this category are wide variations. There may or may not be associated psychoneurotic phenomena. It is possible to make an unlimited series of subtypes of the psychopathic personality. We have selected seven: inferior, alcoholic, affective, aggressive, criminal, schizoid and miscellaneous types. As these subtypes are not discussed in the present study, they are not defined here.

Neurotic Personality.—A person whose behavior and experience are substantially affected by the existence

of traits or symptoms which characterize the generally accepted psychoneurotic syndromes of neurasthenia, hypochondriasis, anxiety neurosis, obsessional neurosis and hysteria.

Personality Variant.—A person who, while not psychotic, frankly psychoneurotic or psychopathic, has appreciably more weighting of the personality than the average normal subject. Such patients represent deviations from the average. The personality bias includes such traits as timidity, egocentricity, irritability, cantankerousness, hypersensitivity, moodiness, emotional lability, solemnity or general light heartedness.

Normal Adult Personality, but with Neurotic Traits in Childhood.—A well adjusted adult with a history of such neurotic traits in childhood as persistence of enuresis beyond infancy, nightmares, sleep walking and temper tantrums.

Normal Personality Except for General Nervousness.—A person of average personality, with some slight or special sensitivity, such as moderate emotional tension or a tendency to mild psychosomatic manifestations—for example, gastrointestinal symptoms, palpitation or perspiration—in association with emotional tension.

Behavior Problem in Childhood or Youth.—Persons who, without manifestation of intrinsic personality disorder (neurosis, psychopathy), had acted in a manner which was in acute conflict with the average standards of performance for his social group. Here would be included patients with a history of an isolated instance of delinquent behavior.

OBSERVATIONS AND CONCLUSIONS

Pretraumatic Personality Status.—The classification of the 200 patients on the basis of the categorical pretraumatic personality status is presented in table 1.

This distribution of personality categories probably represents an average for the portion of the population which is treated in large municipal hospitals. It should be noted that nearly half the number were considered essentially normal; approximately one sixth had psychopathic personalities; about the same number were personality variants, and about one twelfth of the patients had neurotic personalities.

TABLE 1.—*Pretraumatic Personality Status of Two Hundred Patients*

Diagnosis	Number of Patients	Percentage of Total Number of Patients
Normal personality	87	43.5
Psychopathic personality	34	17.0
Personality variant	31	15.5
Neurotic personality	17	8.5
Normal personality except for general nervousness	10	5.0
Mental deficiency	7	3.5
Neurotic traits in childhood	1	0.5
Psychotic behavior	1	0.5
Behavior problem (in childhood or youth)	1	0.5
Pretraumatic personality unknown	11	5.5

Pretraumatic Personality in Relation to Post-Traumatic Mental Symptoms.—The post-traumatic psychiatric symptoms of each patient were carefully studied. It was found that prolonged failure to resume employment showed a higher correlation with the existence of mental symptoms than with any other symptom (headache, dizziness or direct physical sequelae). These post-traumatic mental symptoms have been discussed in detail by an associate.[9] They are mentioned here only for purposes of correlation with personality status. They may be listed and defined as follows:

TABLE 2.—*Distribution of Psychiatric Symptoms in a Series of Sixty-Four Patients with Post-Traumatic Mental Symptoms*

Symptom	Number of Patients
Anxiety states; apprehension	48
Fatigue (neurasthenia)	7
General nervousness	4
Hypochondriasis	2
Obsessive-compulsive neurosis	1
Depression	1
Euphoria	1

Fatigue (neurasthenia): Complaints of tiring easily; a sense of exhaustion and lack of energy, and increased need for rest and sleep.

Nervousness; Inability to Concentrate: Pronounced tension with associated psychosomatic manifestations and inability to concentrate, without anxiety or other clearly neurotic disorder.

Fears; Anxiety; Panics: States of morbid, uncontrollable apprehension, either acute or chronic and of variable degree and duration. There may be associated somatic symptoms, and fatigue and nervousness may be present in addition.

Depression; Apathy: A predominant mood of depression or lack of concern with the usual objects of interest.

Hypochondriasis: Excessive preoccupation with and anxiety about the state of one's health, including specific anxiety about the head.

Obsessive-Compulsive Symptoms: The existence, singly or in combination, of obsessive, ruminative, compulsive, phobic or ritualistic phenomena.

Gross Change in Personality Only: Qualitative and quantitative deviation from pretraumatic patterns of personality and behavior not related to coexisting psychogenic changes, in particular in the absence of post-traumatic anxiety and other psychoneurotic states.

Euphoria: Elated, expansive mood with heightened sense of well-being.

In each case in which the patient showed any mental changes in convalescence the predominant symptoms were arbitrarily selected. Seventy patients (30 per cent) had post-traumatic men-

tal symptoms. It should be emphasized that the predominant mental symptom in convalescence is not the only one; virtually every patient presented more than one symptom. In fact, fatigability was present in a larger total number of patients than was any other symptom. However, it appeared of relatively minor importance, for in only 7 patients did it overshadow the other symptoms. Headache and dizziness were not taken into account.

Of the 70 patients who had post-traumatic mental symptoms, 64 (32 per cent of the total of 200 patients, or 90 per cent of the 70 patients) presented neurotic symptoms. The remaining 6 (3 per cent of the total of 200 patients, or 8.5 per cent of the 70 patients) showed a rather general personality change, without particular neurotic symptoms. Each of these 6 patients with general personality change had suffered an obviously severe injury to the brain, evidenced by such signs as prolonged coma and disorientation, prolonged deficit in performance tests, bloody spinal fluid, focal neurologic signs and indications for operation on the skull.

The distribution of the predominant psychiatric symptoms in our 64 cases is given in table 2.

The pretraumatic status of personality is correlated with the post-traumatic status in table 3.

From table 3 the following figures are taken for purposes of comparison:

Patients Presenting Post-Traumatic Mental Symptoms:

36% of 17 patients with pretraumatic neurotic personality.
35% of 34 patients with psychopathic personalities
30% of 31 patients with personality variants
29% of 7 patients with mental deficiency
30% of 87 patients with normal personality

These figures indicate that there is little, if any, correlation between the pretraumatic personality and the post-traumatic psychiatric symptoms. They certainly indicate that the pretraumatic personality is not a dominant factor in the production of post-traumatic symptoms.

It may be argued that a figure of 36 per cent for "neurotic" persons and of 35 per cent for "psychopaths" is significant as compared with a figure of 30 per cent for the entire series of 200 patients and for the group of 87 normal patients. While the small difference may be significant, it is certainly not sufficiently great to support any theory of post-traumatic neurosis which places the chief emphasis on the sole factor of pretraumatic personality. It should be noted that the highest incidence of post-traumatic mental symptoms (50 per cent) occurred in a group of 10 patients who were characterized as "essentially normal except for general nervousness."

The statements in the foregoing statistical analysis do not mean that the pretraumatic personality is never responsible for symptoms. In a particular case specific features of the pretraumatic personality may be the chief factor in the production of symptoms. But a comprehensive diagnosis of pretraumatic personality (such as "neurotic" or "normal") is not specific enough to indicate any probability of post-traumatic mental symptoms. This is supported by our observation that the highest incidence of symptoms appeared in the patients who were considered "essentially normal except for general nervousness." Of the total series of 200 patients, there were approximately 20, or 10 per cent, whose pretraumatic personality appeared to be of major significance in the production of post-traumatic mental symptoms. However, not more than 6 of these patients (3 per cent) were neurotic. Thus, while in certain cases the pretraumatic personality was believed to play a major role, the specific items were too subtle for generalization.

Relation Between Categorical Diagnosis and Clinical Impression.—Although the pretraumatic personality is generally not the sole factor in the

TABLE 3.—*Correlation of Pretraumatic and Post-Traumatic Personality Status*

		Post-traumatic Personality Status					
		Free from Symptoms		Psychiatric Symptoms		Personality Change Only	
Pretraumatic Personality Status	Number of Patients	Total Number of Patients	Per Cent of Patients	Total Number of Patients	Percentage	Total Number of Patients	Percentage
Normal personality	87	61	70	26	30	0	0
Psychopathic personality	34	21	62	12	35	1	3
Personality variant	31	20	65	9	30	2	5
Normal personality with general nervousness	10	5	50	5	50	0	0
Neurotic personality	17	11	64	6	36	0	0
Mental deficiency	7	5	71	2	29	0	0
Neurotic traits in childhood	1	0	0	1	100	0	0
Psychotic behavior	1	0	0	1	100	0	0
Behavior problem	1	0	0	0	0	1	100
Unknown	11	7	64	2	18	2	18
Totals	200	130	65	64	32	6	3

causation of psychologic sequelae, there is little doubt that in many cases it contributes to a greater or lesser degree. In the final review of each case by the entire staff opinions were expressed as to the role of the pretraumatic personality in the production of sequelae. The clinician who handles a case builds up his impression from numerous items and details. The summation of impressions which go into the formation of an opinion are the result of implicit, as well as of explicit, perceptions. These opinions were clinical approximations reached after the event, and not to be confused with the categorical classification of all patients, regardless of the presence or absence of symptoms, dealt with in the preceding section. Since such clinical approximation is the routine approach to the problem in the clinic, its evaluation in relation to the present series of patients may be useful.

The full staff was in general agreement that the pretraumatic personality played some part in the production of psychologic sequelae in 58 (80 per cent) of the total of 70 patients with such sequelae. Reference to table 3 shows that approximately one half (26) of these patients had pretraumatic "normal" personalities and 32 had pretraumatic abnormal personalities. Virtually the same proportion is found among the 130 patients who did not have psychologic sequelae: The personalities of 61 were diagnosed as normal and those of 57 as abnormal (5 were mentally defective, and the previous personality of 7 patients was unknown).

Work History.—As Lewis [3] stated that the work history is of relevance in evaluation of pretraumatic personality, comment is pertinent. In the present series 146 patients had a satisfactory work history as judged by steadiness and continuity of employment, and 41 patients had an unsatisfactory work history. Of the 146 patients with a satisfactory work history, 93 (63 per cent) had no post-traumatic mental symptoms, and 53 (37 per cent) had such symptoms. Of a total of 41 patients who had no steady employment or had other unsatisfactory work records, 26 (63 per cent) had no psychiatric symptoms after injury, and 15 (37 per cent) had such symptoms. Thus the percentages are identical for the two groups and indicate that in itself the work history bears no relation to the presence or absence of post-traumatic mental symptoms.

Psychiatric Family History.—In discussing the liability of a personality to react, Symonds and Russell [1b] used the term "predisposition." They included not only the pretraumatic personality of the patient but the psychiatric history of his antecedents. In the present series there were 37 patients whose family histories gave evidence of neurosis, alcoholism, psychopathic personality, psychosis or similar disturbance. Of these, 26 (70 per cent) had no post-traumatic mental symptoms, and 11 (30 per cent) had such symptoms. Of 125 patients without a positive family history, 78 (62 per cent) had symptoms, and 47 (38 per cent) had no symptoms. Thus, there is a difference of only 8 per cent in favor of the development of post-traumatic mental symptoms in persons with a positive family history of psychiatric disorders. This difference is of doubtful significance.

Complicating Psychosocial Factors.—As the present paper is primarily concerned with the potential role of the personality a detailed discussion of the general causation of psychiatric sequelae of head injury is not attempted. It may be pointed out, however, that there was a high correlation between the continuance of psychiatric sequelae and the existence of associated situational factors. The latter included anxiety about returning to jobs in which the head injury had been sustained (firemen), fear in crossing streets, concerns about domestic difficulties, unsettled litigation and complicating injuries and illnesses.

TABLE 4.—*Complicating Psychosocial Factors and Post-Traumatic Mental Symptoms*

Complicating Factors, Regardless of Estimated Influence or Sequelae	Number of Patients	Patients with Symptoms	
		Number	Percentage
Litigation	34	22	64
Domestic troubles	18	7	40
Complicating injuries	28	9	32
Occupational difficulties	11	8	75
Financial difficulties	8	2	25
Selective service	5	2	40

One hundred and four patients presented a variety of complicating factors (table 4).

According to this table, there is a substantial correlation between the existence of litigation, on the one hand, and the development of psychiatric sequelae (64 per cent), on the other. Under "occupational difficulties" one will note that of 11 patients 8 (75 per cent) had sequelae. They were men engaged in a hazardous occupation (firemen) who had witnessed the deaths of some of their fellows. All these patients were receiving full salary while ill. Thus, for them to remain ill meant a continuation of their safe status. In that respect they could be compared to soldiers who had failed to recover. Thus, this group could well be classified with the litigation group, so that a total of 45 patients

had an intelligible motive (conscious or unconscious) for remaining sick, of whom 30 (66 per cent) did have mental symptoms. There is a higher correlation here than with the pretraumatic personality type or with any other factor in this study.

To test a possible chance relation, the pretraumatic personality status was correlated with the existence of complicating factors. From these correlations it appears that complicating factors were presented by 53 (60 per cent) of the 89 "normal" patients, by 10 (59 per cent) of the 17 "neurotic" patients, by 20 (59 per cent) of the 34 "psychopaths," by 22 (70 per cent) of the 31 patients with "personality variant" and by 6 (60 per cent) of the 10 patients with "normal personality except for general nervousness." The average incidence of complications for the entire series of 200 patients was 62 per cent. These figures indicate a distribution which excludes the factor of chance in the conclusion that there is a high correlation between the existence of psychiatric sequelae and psychosocial complicating factors.

COMMENT

No author, to my knowledge, has asserted that the pretraumatic personality is exclusively responsible for the development of psychologic sequelae of head injury. The view that pretraumatic personality may be largely responsible for the psychiatric sequelae of head injuries was epitomized by Symonds with the conclusion that ". . . it is not only the kind of injury that matters, but the kind of head." [8a] Later, Symonds and Russell expressed the conviction that "the mental constitution before injury plays an important part in the prognosis of head injuries." [1b] They mentioned "predisposition to mental disorder . . . evinced by the family or personal history of the individual." In a group of military patients they found that "predisposition" was twice as common among the men with chronic illnesses as among those with short illnesses. Also, twice as many men were invalided from the group with predisposition as from the group which showed no predisposition. They noted, however, that 33 per cent of the group with predisposition to mental disorder returned to active service, that predisposition in itself did not carry a bad prognosis but that among the factors having an adverse effect on recovery from head injury the role of predisposition was of significance. They stated further:

> Our data therefore suggest that if two men of dissimilar mental constitution suffer head injury of comparable severity, as judged by the duration of the PTA [post-traumatic amnesia], the prognosis is much worse for the man with a latent or evinced liability to mental disorder.

Lewis [3] reached a similar conclusion from a study of 64 patients with head injury whose symptoms had persisted so long as to be looked on as chronic and the character of whose symptoms was such that they had been transferred to a "neurosis center." Lewis compared these patients suffering from head injury with 64 neurotic patients without head injury in the same hospital. The latter group had been especially selected to match the group with head injury in that they "exhibited the clinical syndromes in the same proportions as did the head injury cases. Thus, there were 16 patients with conversion hysteria in each group, 2 patients with hysterical amnesia, 6 with a severe acute anxiety state, 14 with a chronic anxiety state, and so on." These groups were compared with respect to a number of attributes of psychiatric interest, including family history, occupational and personal history, previous personality, present illness and symptoms thereof. In evaluation of the previous personality, only twelve types were considered: stable, weak, delinquent, inert, rebellious, suspicious, cyclothymic, schizoid, hysterical, anxious, hypochondriacal and obsessional. Lewis concluded:

> . . . the long-standing, relatively intractable post-contusional syndrome is apt to occur in much the same person as develops a psychiatric syndrome in other circumstances without any brain injury at all.

Lewis took note of possible objections to the use of his group with head injury as representative of the "minor contusional syndrome" (Symonds' equivalent of the term "post-concussion syndrome"). His group had been selected from patients with head injury because of the chronicity of symptoms which were recognized as characteristically neurotic. It is obvious that conclusions derived from a study of such a group cannot be applied to the general group of patients with post-traumatic mental sequelae. But even in his group it was noted that 36 (56 per cent) of the patients with head injury who were invalided because of neurotic sequelae had pretraumatic "stable" personalities, whereas in the group of "neurotic" patients who had not sustained head injury only 25 per cent had had previously stable personalities.

It should be emphasized that neither Symonds nor Lewis ascribed the development of psychiatric sequelae exclusively to a pretraumatic personality. Both pointed out that the reaction of the personality to immediate organic features of the head injury, such as dizziness and head-

ache, was unquestionably a factor, and they also took note of the undoubted influence of complicating situational stresses arising out of or relating to the injury. They also emphasized the motivation, undoubtedly subconscious, which might perpetuate symptoms when recovery from such symptoms would be followed by return to active military service. The chief difference between their observations and the results of the present study relates to the weight to be attached to the pretraumatic personality.

Schilder [5] pointed out, as did Symonds and Russell [1b] and Denny-Brown,[10] that the experiences directly referable to physical trauma to the brain, such as headache and dizziness, in themselves contribute to the development of neurotic reactions. Of additional interest is his insistence that neuroses associated with trauma to the head should be distinguished from neuroses associated with trauma to other parts of the body. He demonstrated that the cause of the two types of neurosis may be quite different; that special value is set by the patient on his head, particularly his brain, and that the physical symptoms associated with head injury (dizziness, instability) produce a sense of insecurity, with associated anxiety. Schilder did not place any special weight on pretraumatic personality. He stated:

> Traumatic neurosis in general, and neurosis after head injuries, may occur in individuals who were neurotic previously or had neurotic tendencies; or it may occur in individuals who were not neurotic in the commonly accepted sense before the accident.

Denny-Brown [10] maintained that persistent disability (sequelae) in the individual case must be evaluated in terms of both physiologic and psychologic factors. He stated:

> Too frequently, emphasis is laid wholly on either structural damage or psychoneurotic state, with consequent failure to achieve the best results from treatment of both. Although particularly evident to the trained neurologist by reason of his familiarity with both functional and organic nervous disorders, the proportions of the mixture should be evident to anyone who takes time to sum up the pretraumatic nervous constitution and personality, the severity of the general brain injury, the residual intellectual and physical state, and the nature and degree of persistent anxiety.

From our data it appears that there is little, or no, correlation between pretraumatic personality and the liability to development of post-traumatic mental symptoms. A patient with a pretraumatic "neurotic" personality may be free from symptoms. A patient with a pretraumatic "normal" personality may be crippled by mental symptoms. This does not mean that the pretraumatic personality may not play a large, or even the sole, part in the production of post-traumatic mental symptoms. It does mean that the development of post-traumatic mental symptoms may not generally be ascribed to the pretraumatic personality. There is no general rule that patients with over-all neurotic or psychopathic personalities are more likely to manifest symptoms after trauma than are normal persons.

SUMMARY

In 200 cases of head injury the categorical pretraumatic personality was found to have little, if any, correlation with the incidence of post-traumatic mental symptoms. There was a significant correlation between the incidence of post-traumatic mental symptoms and the existence of complicating psychosocial factors.

Boston City Hospital.

10. Denny-Brown, D.: The Sequelae of War Head Injuries, New England J. Med. **227**:771-780 and 813-821, 1942.

EFFECT OF SODIUM AMYTAL AND AMPHETAMINE SULFATE ON MENTAL SET IN SCHIZOPHRENIA

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It usually is stated that schizophrenia is characterized by three primary symptoms: a disturbance in attention, a disturbance in the association of ideas and a disturbance in affect. The other features of this disorder are regarded as secondary elaborations of these primary symptoms. The relationships among the primary symptoms and between the primary and the secondary symptoms are of interest from a variety of standpoints: etiologic, diagnostic, prognostic and psychopathologic. Increased interest in these topics followed the reports of Lindemann [1] that sodium amytal injected intravenously in smaller than sleep-producing amounts often caused a profound change in the mental status of a patient, sometimes temporarily changing his reactions to relatively normal ones. Thus, in the case of schizophrenia, the attention may be improved, the thought processes may become more logical and the affect may appear more adequate. There is also an increased ease of communication, so that the patient may reveal the content of his psychosis. Furthermore, under the influence of the drug, some patients show improvement in but one or two of the primary symptoms, and, finally, some patients show little or no change. This drug, then, affords an opportunity to study the relation among the symptoms and to investigate problems of diagnosis, of etiology and of prognosis. For example, Gottlieb and Hope [2] stated that a good response to sodium amytal was related to a favorable prognosis, and Layman [3] reported that the performance of a group of patients on a battery of psychologic tests was improved by the drug. It would be desirable to have quantitative measures of changes in the primary symptoms, so that these problems could be investigated with greater exactness. Some beginnings have been made in this direction. The use of certain psychometric tests has redefined the whole problem of schizophrenic thinking.[4] Similarly, a technic for measurement of reaction time has been developed which may be used to measure the disorder in attention.[5] The present report deals with the question: Can the clinical improvement in attention produced by intravenous administration of sodium amytal in schizophrenic patients be measured by this reaction time technic?

The technic of measuring attention is more specifically referred to as a method of measuring mental set. The latter term is preferable, since it has a more precise meaning than attention. In terms of the experimental technic, mental set means the ability to maintain an orientation toward certain environmental stimuli at a high level. The procedure involves measuring the subject's reaction time to an auditory stimulus under two types of conditions. In one condition a warning or preparatory signal is presented at constant temporal intervals before each reaction signal (regular procedure). In the second condition the length of the preparatory interval between the warning and the reaction signal is varied haphazardly (irregular procedure). In the first condition a normal subject will profit by the constant interval between the two signals and will be prepared to react quickly. In the second condition his reaction times are longer, apparently because he does not know when to expect the reaction signal. Furthermore, in the

1. Lindemann, E.: The Psychopathological Effects of Sodium Amytal, Proc. Soc. Exper. Biol. & Med. **28**:864, 1931; Psychological Changes in Normal and Abnormal Individuals Under the Influence of Sodium Amytal, Am. J. Psychiat. **11**:1083-1091, 1932. Lindemann, E., and Malamud, W.: Experimental Analysis of the Psychopathological Effects of Intoxicating Drugs, ibid. **13**:853-879, 1934. Lindemann, E.: The Neurophysiological Effect of Intoxicating Drugs, ibid. **13**: 1007-1037, 1934.

2. Gottlieb, J. S., and Hope, J. M.: Prognostic Value of Intravenous Administration of Sodium Amytal in Cases of Schizophrenia, Arch. Neurol. & Psychiat. **46**:86-97 (July) 1941.

3. Layman, J. W.: A Quantitative Study of Certain Changes in Schizophrenic Patients Under the Influence of Sodium Amytal, J. Gen. Psychol. **22**:67-86, 1940.

4. Kasanin, J. S.: Language and Thought in Schizophrenia, Berkeley, Calif., University of California Press, 1944.

5. Huston, P. E.; Shakow, D., and Riggs, L. A.: Studies of Motor Function in Schizophrenia: II. Reaction Time, J. Gen. Psychol. **16**:39-82, 1937. Rodnick, E. H., and Shakow, D.: Set in Schizophrenia as Measured by a Composite Reaction Time Index, Am. J. Psychiat. **97**:214-225, 1940.

regular procedure, as the length of the preparatory interval is increased to about fifteen or twenty seconds, the advantage of a constant interval is lost, and the reaction times approximate those of the irregular procedure. Curves plotting reaction time as a function of the preparatory interval show a separation of the curves for the two procedures with intervals below fifteen or twenty seconds in a normal group, the curve for the regular procedure representing faster reactions than the curve for the irregular procedure. Schizophrenic subjects, on the other hand, fail to profit by a knowledge of the length of the preparatory interval to the same degree that normal subjects do. As a consequence, similar curves for a schizophrenic group show a separation of the curves for the regular and the irregular procedure only for intervals below about five seconds. With longer preparatory intervals curves for the patients tend to run together. Hence it has been suggested that schizophrenic patients do not maintain a mental set as well as normal persons.[5]

MATERIALS AND METHODS

Nine schizophrenic patients and 9 normal control subjects were used in this study. The patients had all been recently admitted to the Iowa State Psychopathic Hospital, though the average duration of the psychosis was nine months. They had a mean age of 28.5 years, with a range from 16 to 49 years. Two were women and 7 were men. The clinical subtypes were distributed as follows: paranoid, 1; hebephrenic, 3; simple, 1, and unclassified, 4. All the patients were in good contact with the environment and were cooperative in the experimental situation. The control subjects were university students. Their mean age was 22.8 years, with a range from 20 to 26 years. Six were women and 3 were men.

The apparatus consisted of a flashlight bulb to serve as a warning signal, a buzzer to which the subject reacted by slipping his index finger off a telegraph key, an electrical chronoscope calibrated in hundredths of a second to measure the reaction time and a device to control the length of the preparatory intervals. This device was a synchronous motor polygraph which drove a punched paper tape. Completion of an electrical circuit through holes in the tape flashed the warning light and, at the end of the proper preparatory interval, sounded the buzzer. Simultaneously with the sounding of the buzzer the chronoscope started. It was stopped when the subject reacted. Five preparatory intervals were used: two, three and a half, five, ten and twenty seconds. These were presented in two ways. In the regular procedure all the reactions to any preparatory interval were given together. The order of presentation by intervals was: three and a half, ten, five, two and twenty seconds. Twenty reactions to each interval were taken. After each group of twenty reactions, the subject was told a new interval was to be used. In the irregular procedure the preparatory intervals were presented at random until twenty reactions to each interval were obtained. In this procedure the time between a reaction and the next warning signal also varied. Practice sessions of ten reactions were given before both the regular and the irregular procedure. The instructions to the subject were worded so as to orient him toward the reaction movement rather than the stimulus, since "muscular" reactions are shorter and less variable than "sensorial" reactions.[6] Rest periods of about two minutes were given after each twenty reactions in both procedures. Each procedure took about forty-five minutes. The irregular procedure was performed before the regular one in each session.

Each subject was tested four times: In sessions 1 and 2 there was no medication. In sessions 3 and 4 each subject received 250 mg. of sodium amytal and 10 mg. of amphetamine sulfate intravenously. The latter drug combats the sedative effect of sodium amytal, so that more time-consuming experiments may be performed.[7] It should be noted that a maximal effect in each subject with a standard dose of the drugs would not be expected. However, the present study was preliminary, and it was thought that if changes in mental set could be measured by the suggested technic, the effect should be revealed with somewhat smaller than maximal doses. After the drugs were injected, a period of thirty minutes was allowed for the acute effects to wear off. In the final analysis of the results, session 2 (without amytal) was compared with session 4 (with amytal). This was done to yield somewhat less variable material. Session 1 seemed to show some practice effects, as did the first session with amytal (session 3). However, the general picture of the results remained the same regardless of what sessions with or without amytal were used for comparison. Owing to tearing of the punched paper tape on humid days and occasional failure of a subject to hold the telegraph key down for subsequent reactions, twenty reactions per preparatory interval were not obtained for every subject. Thus, from fifteen to eighteen reactions per interval were used in the statistical analysis, with each subject serving as his own control with respect to the number of reactions per interval. The average number of reactions per interval for all subjects was seventeen.

RESULTS

Without Drugs.—The performances of the two groups can be compared by examination of table 1 and figure 1, in which means for the group, standard deviations of the means and mean coefficients of variation are tabulated and plotted for the condition without amytal.

From this material it may be seen that the mean reaction time of the patient group is longer than that of the control group in both procedures for all preparatory intervals. The differences between the two groups are statistically significant at the 1 per cent level of confidence at each preparatory interval for the corresponding procedures.

A more interesting comparison is that the curves for the two procedures in the patient group cross, while in the normal group the curves are separate for all preparatory intervals, the means

6. Woodworth, R. S.: Experimental Psychology, New York, Henry Holt & Company, Inc., 1938, pp. 306-308.

7. Gottlieb, J. S., and Coburn, F. E.: Psychopharmacologic Study of Schizophrenia and Depressions, Arch. Neurol. & Psychiat. **51**:260-263 (March) 1944.

for the regular procedure being always shorter. In the patient group at the two second interval the difference in the two procedures yields a statistical level of confidence of 2 per cent, but at all other intervals the differences are not significant enough to warrant statistical confidence. These figures are 2, 40, 60, 20 and 80 per cent for the two, three and a half, five, ten and twenty second intervals respectively. For the control subjects, on the other hand, the levels of confidence for the differences between the two procedures are 1, 1, 2, 5 and 70 per cent for the two, three and a half, five, ten and twenty second intervals respectively. These levels of confidence for the control group are a reflection of the fact that as the preparatory interval increases in length the means of the regular procedure approach those of the irregular procedure.

These findings confirm the results of previous experiments of this type.[5] They are interpreted to mean that normal subjects are able to maintain the set to react at a higher degree when a preparatory interval of constant length (regular procedure) is used than when the preparatory interval varies haphazardly (irregular procedure). As the interval increases in length, however, it becomes increasingly difficult to hold the set to react at a high level of preparation, and the means of the regular procedure approach those of the irregular procedure. In the patients, on the other hand, the ability to maintain the set to react is poorer; the differences between the means of the procedure are less at the shorter intervals than those for the control subjects, and the curves of the two procedures join or cross at shorter intervals (fig. 1).

With Drugs.—The behavior and the spontaneous comments made by each subject during the amytal sessions were recorded. After injection of the drugs the control subjects complained of light headedness, blurring of vision and slight numbness and weakness of the arms and legs. Their gait was somewhat unsteady and speech was slow and slurred. They were extremely talkative and stated that they felt less motivated to do well in the experiment and that it was more difficult to keep oriented toward the task. The patients complained of similar initial changes, but they verbalized these less than the control subjects. Objectively, they were more talkative and seemed to have increased social and self confidence after injection of the drugs. Their speech content tended to be more relevant, their attention better and their affect warmer.

TABLE 1.—*Mean Reaction Times, Standard Deviations and Mean Coefficients of Variation in Hundredths of a Second by Preparatory Intervals for Regular and Irregular Procedures Without Sodium Amytal*

	Preparatory Intervals														
	2 Seconds			3.5 Seconds			5 Seconds			10 Seconds			20 Seconds		
	Mean	S. D.	C. V.	Mean	S. D.	C. V.	Mean	S. D.	C. V.	Mean	S. D.	C. V.	Mean	S. D.	C. V.
Patient Group															
Regular procedure	31.66	6.85	12.91	32.33	5.16	14.53	33.10	6.92	12.15	36.12	7.61	15.24	35.56	6.90	16.30
Irregular procedure	33.62	5.48	16.26	33.27	5.29	16.16	33.67	5.73	14.74	33.70	5.75	17.41	35.22	6.43	14.45
Control Group															
Regular procedure	20.13	2.80	14.80	21.18	2.98	13.20	22.44	4.02	13.49	23.06	3.83	14.25	25.25	4.05	12.03
Irregular procedure	26.88	2.82	14.30	25.41	2.85	12.40	25.47	2.99	12.15	25.84	2.51	13.54	25.73	2.61	14.78

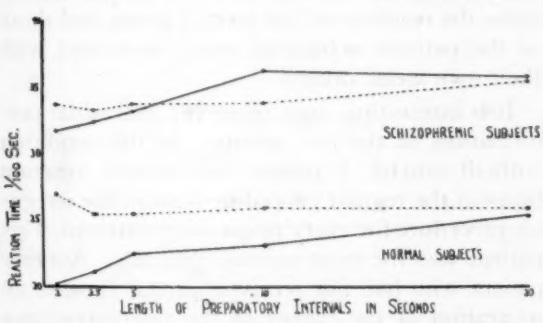

Fig. 1.—Mean reaction times of schizophrenic and normal subjects without sodium amytal. In this figure, and in figure 2, the curve for the regular procedure is an unbroken line; the curve for the irregular procedure, a broken line.

Table 2 and figure 2 present the mean reaction times, the standard deviations of the means and the mean cofficients of variation by intervals for both procedures with amytal.

The effect of the drug in the normal group was to increase the reaction time in both procedures for every preparatory interval. The shortest reaction times were found in this group with the shortest preparatory intervals of the regular procedure. The curve of the regular procedure shows a tendency to rise as the preparatory intervals increase. The mean values for the irregular procedure are everywhere longer than those for the regular procedure. The differences between

the means of the two procedures have statistical levels of confidence of 1, 1, 5, 20 and 10 per cent for the one, two, three and a half, ten and twenty second intervals respectively. In general, then, the normal group produced curves of the means with amytal very similar to those without amytal except that both curves with amytal represented slower reaction times than the curves without amytal. This is interpreted as meaning that under amytal sedation these subjects were still able to profit by a constant preparatory interval and reacted more quickly than with random variations of the preparatory interval.

In the group of patients the curve of the regular procedure shows a gradual rise with increasing length of the preparatory interval. The curve of the irregular procedure is practically flat. The point of special interest about these curves is that they are separate for all preparatory intervals, producing a picture similar to that for the control subjects. The statistical levels of confidence which attach to the differences in means of the two procedures are 2, 20, 10, 20 and 5 per cent for the two, three and a half, five, ten and twenty second intervals respectively. These values are in considerable contrast to those found in the condition without amytal.

Is the separation of the curves of the patient group primarily caused by a change in the regular or in the irregular procedure? Examination of the mean values shows that the principal effect of the amytal was to shorten the reactions in the regular procedure to the longer intervals, i. e., to the five, ten and twenty second intervals, while the reactions to the two and three and a half second intervals revealed little difference between the situation with amytal and that without amytal. In the irregular procedure there was a slight tendency for the means to be longer with than without amytal. These results seem to indicate that the patients were able, under the influence of the drug, to profit primarily from the constant preparatory intervals and to maintain a better readiness to react.

Examination of the standard deviations of the means (tables 1 and 2) indicates that the patients as a group showed more variability for all intervals than did the control subjects. In both groups the effect of amytal was to increase the variability for all intervals in both procedures. The means of the coefficients of variation, which express variability in relation to the magnitude of the means, indicate that the effect of amytal was to make the reactions of the control group and those of the patients somewhat more consistent with their own mean values.

It is interesting, also, to survey individual performances in the two groups. In the condition without amytal, 1 patient had shorter reaction times in the regular procedure than in the irregular procedure for every preparatory interval. This patient was the most normal clinically. Another patient who had not received amytal showed no separation of the curves of the two procedures for either short or long intervals. For the remaining 7 patients the curves for the shorter intervals were separated but those for the longer intervals were merged. With amytal, however, 5 patients had separation of the curves of the two procedures for all intervals; 2 patients, for every interval but one, and 2 patients, for three of the five intervals. Of the control subjects without

TABLE 2.—*Mean Reaction Times, Standard Deviations and Mean Coefficients of Variation in Hundredths of a Second by Preparatory Intervals for Regular and Irregular Procedures with Sodium Amytal*

	Preparatory Intervals														
	2 Seconds			3.5 Seconds			5 Seconds			10 Seconds			20 Seconds		
Patient Group	Mean	S. D.	C. V.	Mean	S. D.	C. V.	Mean	S. D.	C. V.	Mean	S. D.	C. V.	Mean	S. D.	C. V.
Regular procedure	31.78	8.41	11.17	32.34	8.44	10.77	32.35	8.33	10.75	32.93	8.13	10.86	33.46	7.88	13.36
Irregular procedure	35.87	7.19	13.01	33.82	7.26	11.10	34.62	8.05	12.81	34.78	7.54	12.10	35.95	7.11	15.55
Control Group															
Regular procedure	23.02	4.30	14.49	23.76	4.90	12.64	24.41	5.46	10.52	25.97	5.59	12.89	26.33	5.13	11.17
Irregular procedure	25.84	5.31	14.61	27.83	5.41	13.21	28.28	5.25	13.21	28.04	5.29	13.09	28.69	5.07	13.24

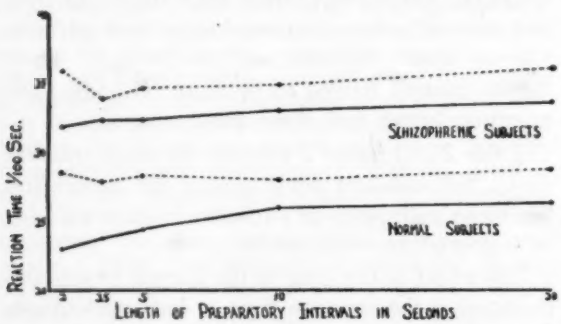

Fig. 2.—Mean reaction times of schizophrenic and normal subjects with sodium amytal.

amytal, the curves for 3 were separated for all intervals; for 3 others, through the ten second intervals, and for 1 through the five second interval. The curves for 1 control subject tended to merge after the three and a half second interval, and for 1, after the two second interval. Of the control subjects with amytal, the curves were separated throughout for 6, through the ten second interval for 1 and through the five second interval for 2.

SUMMARY AND CONCLUSIONS

The present experiment was performed in an attempt to quantify the improvement in attention (mental set) observed clinically in schizophrenic patients who have received intravenous injections of sodium amytal. The auditory reaction time was obtained under two types of conditions. In one condition, the regular procedure, the length of the preparatory interval, i. e., the time between a visual warning signal and the auditory reaction stimulus, was constant for all the reactions to that interval. In the second condition, the irregular procedure, the length of the preparatory interval varied haphazardly. Five preparatory intervals were used: two, three and a half, five, ten and twenty seconds. Nine schizophrenic patients and 9 normal persons served as subjects. Each subject was tested with and without intravenous administration of 250 mg. of sodium amytal and 10 mg. of amphetamine sulfate.

Our results confirm the work of earlier investigations in which no drugs were used. The reaction time of the patient group was significantly longer than that of the control subjects in both procedures. The control group reacted more quickly in the regular procedure than in the irregular procedure for all preparatory intervals. The patient group failed to react more quickly in the regular procedure after the five second preparatory interval. With medication the normal group continued to react more quickly in the regular procedure than in the irregular procedure for all preparatory intervals. The patient group, with medication, had reaction times which were significantly longer in both procedures than those of the control group. However, in contrast to their behavior without medication, they now reacted more quickly in the regular procedure than in the irregular procedure for every preparatory interval.

It is concluded from these results, first, that the schizophrenic patients as a group suffer from inability to attain as high a level of mental set as do normal subjects and that they do not maintain the level of preparation they attain as long as controls. Second, the reaction time technic may be used to measure one aspect of the improvement seen clinically (improvement in attention) in schizophrenic patients when sodium amytal is injected intravenously. Third, the improvement is such as to produce a normal relationship between the reaction times of the regular and those of the irregular procedure.

Dr. J. R. Knott assisted in constructing the apparatus, and Dr. C. R. Strother gave statistical advice.

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EFFECTIVENESS OF DIPHENYLHYDANTOIN IN MANAGEMENT OF NONEPILEPTIC PSYCHOMOTOR EXCITEMENT STATES

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The present report is based on an investigation by Kalinowsky and Putnam [1] which revealed that diphenylhydantoin sodium is capable of producing distinct changes in behavior in nonepileptic psychotic patients. In view of the observations of Blair, Bailey and McGregor [2] and of McEachern,[3] who found that this drug could transform querulous, moody and irritable epileptic patients into pleasant, agreeable and congenial persons, it seemed appropriate to study the effect of diphenylhydantoin on certain mental symptoms of other origin. Kalinowsky and Putnam selected 60 patients representing chiefly cases of schizophrenia and manic-depressive psychosis. The duration of the treatment was from two to five weeks, during which time all other therapeutic methods, including psychotherapy, were purposely omitted, so that the effects of diphenylhydantoin could be accurately observed. The initial daily dose was usually 3 to 4 capsules of diphenylhydantoin sodium, 0.1 Gm. (1½ grains) each. After two days the dose was increased to 5, and later to 6, capsules daily. Improvement occurred in more than 50 per cent of the patients during the period of treatment. This improvement was manifested by diminution of excitement and psychomotor hyperactivity almost irrespective of the type of psychosis. The authors concluded that diphenylhydantoin sodium has a purely symptomatic action on states of excitement in various psychoses and recommended further study of the usefulness of the drug for psychotic states.

PRESENT INVESTIGATION

The following report is based on a prolonged observation of the behavior patterns of a variety of nonepileptic psychotic patients who were treated with diphenylhydantoin sodium. It was originally intended to select a large group of patients consisting of clinic patients under treatment for various psychoneurotic states of tension and excitement and of hospital patients representing the major psychoses. This plan, however, had to be abandoned, since a number of selected clinic patients did not report regularly enough to permit reliable conclusions. Furthermore, a proper evaluation of the effect of the drug on a number of hospital patients proved difficult because the behavior pattern of these patients was not well enough known. Kalinowsky and Putnam stressed the difficulty of judging results in treatment of mental disorders. Since many states of excitement in psychotic patients subside spontaneously, it is often impossible to attribute favorable responses to the specificity of a drug or of any kind of treatment. It was therefore decided to obtain the highest possible degree of accuracy in evaluating the effect of diphenylhydantoin by selecting a smaller number of patients and studying their behavior pattern previous to, during and following treatment with the drug.

Forty patients were chosen for this investigation, which lasted one year. Special behavior charts were devised to register every kind of activity and change in attitude on a daily basis. Every patient was seen twice daily, and additional observations were made by the specially instructed ward nurses. Capsules of diphenylhydantoin sodium, 0.1 Gm. (1½ grains) each, were used exclusively. The importance of individualizing the dose of the drug was soon recognized. The initial daily dose varied from 3 to 5 capsules. In cases of acute manic or catatonic excitement the larger dose was used at the start of the treatment. In cases of less acute excitement the dose was gradually increased from 3 to 6 capsules over a period of from three to six days. The maximum daily dose was 6 capsules.

The average duration of the treatment was from two to five weeks. The patients who showed the best responses had repeated courses of treatment with the drug during the year of observation. The repetition of the treatment seemed the best method of eliminating coincidental factors from evaluation of the effectiveness of the drug.

For the 40 selected patients the following diagnoses had been made:

Manic-depressive psychosis, manic type	6
Schizophrenia, catatonic type	14
Schizophrenia, paranoid type	7
Schizophrenia, hebephrenic type	4
Mental deficiency, excitement states	6
Dementia paralytica, excitement states	2
Postencephalitis, excitement state	1
	40

From Delaware State Hospital.

1. Kalinowsky, L. B., and Putnam, T. J.: Attempts at Treatment of Schizophrenia and Other Nonepileptic Psychoses with Dilantin, Arch. Neurol. & Psychiat. **49**:414 (March) 1943.

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The patients were chosen according to the presence of phenomena of psychomotor excitement, which they had in common regardless of the type of psychosis. The selection was arbitrary, as many patients who would have been excellent subjects for this study had to be excluded because they did not cooperate well enough to take the drug regularly. In the following analysis of the data of this study, more emphasis is placed on the types of responses than on statistical evaluation of the material. A purely statistical analysis would not do sufficient justice to the differences in the individual psychopathologic phenomena and would be handicapped by the relatively small total number of patients. The experience with these patients leads to the conclusion that it is the quality of responses rather than the number of improved patients which provides material for evaluation of the efficacy of diphenylhydantoin sodium in the treatment of nonepileptic psychoses.

ANALYSIS OF DATA

Affective Psychosis.—Of the group with manic-depressive psychoses, 4 patients showed doubtful responses. Manic excitement disappeared during the weeks of treatment with diphenylhydantoin; the improvement, however, was neither prompt nor necessarily specific, since each of these patients showed spontaneous remissions of manic attacks during the one year period of observation. The fifth patient responded promptly and had complete disappearance of manic excitement; the manic phase was followed almost immediately by a depression, which did not respond to diphenylhydantoin. The sixth patient, differing from the others in the manifestations of the psychosis, showed a most favorable response to the drug, which proved to be specific, as could be demonstrated during four courses of the treatment. This case will be described in detail because it illustrates some essential facts about the type of patient who is most responsive to diphenylhydantoin.

Case 1.—The 54 year old white woman, M. A., had been in a perpetual state of pronounced motor restlessness since she was admitted to the Delaware State Hospital, four years prior to this report. She was born in Poland, and facts about her personal and family history are scant. She is known to have been restless, moody and irritable throughout her life. After the death of her husband, in 1940, she became overactive and began to talk in a flighty and irrelevant fashion. She sang and danced almost constantly, refused to go to bed at night, became generally unmanageable and was admitted to the Delaware State Hospital Feb. 26, 1941. On admission she appeared elated, was very restless and sang, danced and exposed herself on every possible occasion. She grew steadily more excited and had to be transferred to a ward for disturbed patients. Neither hydrotherapy nor metrazol or electric shock therapy influenced the excitement state effectively. It became necessary to restrain her and to control her immense restlessness with strong doses of sedatives, as she would climb up window screens and turn somersaults with such violence that she sustained bruises and abrasions all over her body. She masturbated excessively in an exhibitionistic manner.

Medication with diphenylhydantoin sodium was initiated with 4 capsules, but the dose was increased to 6 capsules within three days. Her condition remained without significant change for the first eight days and then showed a steady decrease of motor activity. Restraints became unnecessary as the patient was able to sit in a chair without signs of restlessness. She cooperated well for the first time since her admission to the hospital. Other phenomena of her psychosis, such as elation and flightiness of associations, remained unchanged. This striking improvement was not maintained for more than four or five days after the medication was discontinued. She again became extremely disturbed and remained so in spite of another course of electric shock treatment. Treatment with diphenylhydantoin was resumed after an interval of two months; again the patient showed prompt improvement. Two more courses of treatment with the drug were given, and equally satisfactory results were obtained, as psychomotor disturbances were notably decreased and the patient was able to adjust to the ward life while being treated with the drug. Since no spontaneous remissions occurred at all, the disappearance of psychomotor excitement can be attributed to the specific action of diphenylhydantoin.

Schizophrenic Psychosis.—Kalinowsky and Putnam obtained the best responses with catatonic excitement states. The same observation was made in this investigation. Catatonic patients with sudden outbursts of assaultive and destructive behavior, with screaming spells or sexual excitement, reacted by far more favorably than patients with predominantly negativistic, stuporous behavior, who were essentially uninfluenced. In the schizophrenic group, 3 patients showed pronounced improvement; 3, moderate improvement, and the rest failed to exhibit any appreciable change in behavior. Closer study of the phenomena of the psychoses of these patients suggests that persons whose psychomotor excitement is caused by the fundamental, primary disturbance of the disease process react more favorably than those whose excitement state is a reaction to the accessory, psychogenic factors. The following case represents such a type of primary psychomotor excitement.

Case 2.—The 36 year old white woman, R. C., had been in the Delaware State Hospital since Nov. 6, 1930. The family history is noncontributory except for the fact that her father is described as "excitable and peculiar." As a young girl the patient was reserved and shy and showed early signs of increasing introversion. She became seclusive after leaving school, had spells of complete withdrawal and expressed bizarre and persecutory ideas. Temper tantrums and fainting spells are mentioned in her history. In the hospital she frequently had states of psychomotor excitement. During the past few years she had been mute, assumed rigid postures, masturbated excessively and screamed wildly

when approaching orgasm. She was always extremely tense and attacked other patients in an explosive fashion. There was no favorable response to shock treatments.

Treatment with diphenylhydantoin sodium was started with 5 capsules daily. The amount was increased to 6 capsules daily within three days, and this dose was maintained for four weeks. The patient went into a state of catatonic stupor and had complete disappearance of psychomotor activity. She stopped masturbating and remained completely passive. When medication was discontinued, she again showed all the features of catatonic excitement. Another course of treatment with the drug was started after an interval of two months; again, an almost total disappearance of psychomotor activity was observed. Diphenylhydantoin stopped the urge to masturbate, a practice in which the patient had been engaged almost constantly and which had proved refractory to hydrotherapy, shock treatments and administration of sedatives. The impression was conveyed that excessive masturbation in this case was primarily a symptom of the generalized psychomotor excitement and to only a minor degree an expression of autoerotism. Similar observations during treatment with diphenylhydantoin were made on a number of patients.

The paranoid patients did not show any significant improvement. In this group the excitement was usually a secondary reaction to manifestations of the psychosis, to ideas of persecution or to auditory or visual hallucinations and remained uninfluenced by treatment with diphenylhydantoin. Daily observations on these patients showed such variety in precipitation and duration of excitement states that in the few cases in which a decrease of excitement occurred during the period of treatment it did not seem justified to give the credit to diphenylhydantoin.

Of the hebephrenic patients, 1 showed moderate improvement. This woman was overactive, gave silly performances of dancing and grimacing and showed occasionally assaultive tendencies. During treatment with diphenylhydantoin she became distinctly more passive and appeared preoccupied. The course of treatments could not be repeated, as the patient, again overactive and silly, refused to take the drug regularly.

Excitement States Accompanying Mental Deficiency.—For six patients the diagnosis of mental deficiency with psychosis was made. For psychiatric purposes, this classification lacks differentiation of the psychopathologic manifestations. It seems appropriate, therefore, to subclassify these patients according to the behavior type. Two were hebephrenic; 2 were catatonic; 1 was paranoid, and 1 was manic. All the patients had excitement states. The results of treatment with diphenylhydantoin were variable and not distinctly convincing in 5 patients. However, an excellent result was obtained with the manic patient, whose case will be presented in detail.

Case 3.—The now 45 year old white woman, M. T., was admitted to the Delaware State Hospital on Oct. 8, 1937. The family history revealed several cases of alcoholism and mental deficiency. The patient was always restless but became especially irritable during the menstrual period. She became increasingly restless and talked continuously but was kept at home as long as the family was able to supervise her. After the death of the mother, however, she became actually disturbed, refused to go to bed at night and kept the family awake through constant talking. On admission she appeared agitated, elated, untidy and assaultive and had to be put in a ward for disturbed patients. She became somewhat more cooperative during the years after her admission, but she remained restless and noisy. She was unable to sit still, rocked back and forth, talked in a rambling fashion and produced screaming or barking noises in a staccato fashion.

Treatment with diphenylhydantoin was started with 4 capsules daily, and the dose was increased to 6 capsules within three days. A steady decrease of restlessness and noisiness was observed, and within a week the patient appeared more controlled than at any time prior to the treatment. On the twenty-second day of the treatment a generalized macular exanthem developed, and she complained of pruritus. The temperature and the blood count remained normal. Administration of diphenylhydantoin was discontinued, and the skin cleared in a few days. The improvement in behavior did not last for more than three to four days after the drug was discontinued. A second course of treatment with diphenylhydantoin was started after three months, but the daily maintenance dose was reduced to 4 capsules. Again, she responded favorably, as restlessness and noisiness disappeared within ten days. She still talked to herself and remained somewhat elated and flighty, but she was not disturbed. Medication was discontinued after twenty-six days because she complained of dizziness and itching sensations. A third course of treatments was again successful but had to be discontinued after three weeks, as she again complained of dizziness and became ataxic. Improvement of behavior never lasted longer than a few days after medication was discontinued. Except for her apparent idiosyncrasy to diphenylhydantoin, the patient responded most favorably to the treatment. This result was undoubtedly due to the specific action of the drug, since she had not shown similar improvement either spontaneously or with other treatments.

Organic Psychosis.—Three patients with an organic type of psychosis, 2 with dementia paralytica and 1 with a postencephalitic behavior disorder were included in this investigation because they showed pronounced psychomotor disturbances. One of the patients with dementia paralytica, who was generally deteriorated, went through phases of manic excitement. No definite improvement was observed during treatment with diphenylhydantoin. The other patient with dementia paralytica was rather dull and listless but had frequent spells of excitement and screaming, which seemed to represent reactions to hallucinations. Diphenylhydantoin did not improve this condition. The patient with a postencephalitis disturbance was given the drug because of the unsatisfactory results with scopolamine and other related drugs. Diphenylhydantoin sodium was administered alone and in addition to scopolamine. No improvement occurred with either type of medication.

COMMENT

Kalinowsky and Putnam concluded that diphenylhydantoin sodium has an effect on disturbances of mood, not only in epilepsy but in various other types of psychoses, and they expressed the belief that this fact contributes to the accumulating evidence of a chemical concept of both epilepsy and the major psychoses. The organic concept of these psychoses has been supported by various recent electroencephalographic studies. It would have been desirable to study the electroencephalographic patterns of the patients prior to, during and after treatment with diphenylhydantoin in order to gain a more objective knowledge of the cerebral dysfunction and of the influence of this drug on abnormal electroencephalographic rhythm. It appeared, however, most difficult to find a practical solution to the problem of obtaining reliable records from disturbed and uncooperative patients. Some essential facts about the specific action of diphenylhydantoin were determined by correlating psychopathologic phenomena with positive and negative reactions to the drug. It was emphasized earlier in this report that a merely statistical evaluation of the results of this study would be misleading because it would not do justice to the striking differences in psychopathologic symptoms. From a quantitative viewpoint, only a small number of patients showed favorable results. A qualitative analysis of the cases, however, seems to indicate that a certain type of patient reacts in a specific fashion to diphenylhydantoin. The advantage of the one year period of observation was twofold: Spontaneous remissions were excluded by a repetition of the course of treatments, and an intimate knowledge of the individual symptoms of every patient was gained. This knowledge of the behavior patterns of the patients provided the basis for a more thorough understanding of the nature of the excitement states. It soon became evident that the action of diphenylhydantoin on states of excitement is not symptomatic per se but depends on the nature of the excitement state. Only excitement states which seemed to be caused by the fundamental factors of the psychosis reacted to the drug, whereas states of excitement representing reactions to secondary, i. e., psychogenetic, factors remained uninfluenced. It is not overlooked that reactions of the second type are psychopathologic phenomena, expressing a particular person's way of adjustment to a certain situation. The excitement of the first type, however, seems to be caused by a more fundamental, i. e., pathophysiologic, disturbance. One is led to believe that states which react favorably to diphenylhydantoin belong exclusively to this type. This observation gives support to the concept of the "fundamental disturbance" in the psychoses which was introduced by a number of authors, notably, Bleuler,[4] Birnbaum[5] and Küppers.[6] Further objective evidence in this direction can be found in electroencephalographic studies of Finley,[7] who succeeded in obtaining tracings during and between psychotic episodes. He reported, for instance, a case of catatonic excitement in which rapid frequency occurred during a state of emotional turmoil and decreased notably when the condition was in remission.

Interesting observations were made with intravenous injections of sodium amytal. Patients with excitement states of the primary type showed no significant change in talk or behavior while under the influence of sodium amytal, but patients whose excitement states were reactions to psychogenic factors often appeared considerably relaxed and more responsive. This observation supports the belief that in treatment with diphenylhydantoin the hypnotic action can be disregarded.

Electric shock therapy did not seem to be favorably influenced by previous treatment with diphenylhydantoin. Kalinowsky and Putnam reported that subsequent electric shock treatments in several instances led to a remission after only one convulsion, and they planned systematic attempts at medication with diphenylhydantoin prior to shock treatment. According to experience with patients selected for this investigation, previous treatment with diphenylhydantoin rendered the patient more resistive, and duration of shock and voltage often had to be increased. The number of convulsions needed before improvement took place was not decreased and varied greatly.

If one observes psychotic patients daily for a year, one cannot fail to notice that many types of favorable changes occur spontaneously, and one becomes progressively immune to therapeutic positivism. Many cases, thought to be therapeutic successes, were disregarded because the patients showed equally favorable reactions during the intervals between treatments. On the

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other hand, greater significance could be attributed to the cases in which the reaction could be considered positive after all coincidental factors had been eliminated, because here it was certain that diphenylhydantoin exerted a specific influence.

In his discussion on the paper in which he reported diphenylhydantoin sodium to be an effective anticonvulsant, Putnam [8] stressed the fact that there were several kinds of convulsions and suggested that there should be several types of medication to control them. It now seems that there are different kinds of nonepileptic psychomotor excitement states, some of which are caused by pathophysiologic disturbances and can be controlled with diphenylhydantoin. Further studies on the usefulness of this drug for these specified psychotic states promise to contribute to the chemical treatment of the psychoses, as well as to the further clarification of an organic concept of the major psychoses.

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THE HUMAN PYRAMIDAL TRACT

XI. CORRELATION OF THE BABINSKI SIGN AND THE PYRAMIDAL SYNDROME

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The present study is an attempt to correlate the symptoms and signs of the pyramidal tract syndrome with the Babinski reflex. A destructive upper motor neuron lesion involving the pyramidal bundle has been said traditionally to produce the following abnormalities: paralysis of the spastic type; hyperactive tendon reflexes; loss of the superficial abdominal and cremasteric reflexes; appearance of certain pathologic reflexes among which is the extensor toe sign of Babinski, and, finally, absence of the reaction of degeneration in the peripheral nerves. Paralysis, the most important feature of the syndrome, is defined as loss of the power of movement. Evidence is accumulating that the Babinski sign can be elicited by general suppression or inhibition of somatic nerve activity. If the pyramidal tract is entirely involved in the mechanism of production of this extensor toe sign, one can be more specific and say that possibly a physiologic block of nervous energy in the tract is the causative factor. For example, the Babinski reflex can be produced in deep sleep; it can be elicited during a certain stage in the pharmacologic action of such drugs as pentobarbital sodium and scopolamine; prolonged physical exertion predisposes to its appearance; the reflex is present in hypoglycemic shock, it exists potentially in cases of loss of blood in certain quantities from injured vessels, which may be located remote from the site of the central nervous system, and the indications are that a temporary sign may be produced on proper stimulation in some systemic and neurologic diseases. The voluntary striated muscles in many of these situations are merely in a state of flaccid quiescence; and if the causative factor is remedied in time, the extensor toe sign reverts to the normal flexor type, with no residuum of motor deficit. If suppression, as well as destruction, of somatic neurons in the central nervous system is a possible factor in the production of the Babinski reflex in some disease processes affecting the central nervous system, then variable voluntary motor deficits might be expected to occur. The literature has been canvassed for reports of cases in which the Babinski sign was exhibited, in an attempt primarily to test the validity of this assumption.

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MATERIALS AND METHODS

Reports of 1,600 individual cases of the pyramidal tract syndrome in each of which either a unilateral or a bilateral Babinski sign was exhibited were collected from the ARCHIVES, the *Journal of Nervous and Mental Disease* and *Brain*. This sign has been correlated with the reported age and sex; the laterality; the somatic motor deficit; the state of tone of the muscles, and the activity of the tendon, abdominal and cremasteric reflexes.

RESULTS

In 1,008 of the 1,600 cases the condition was chronic; in 480, it was acute, and in 112 cases it could not be classified. The chronicity was determined on the basis of the onset of motor deficit rather than of any other feature of the disease process, whatever it may have been.

In 915 cases the patients were males, in 624 cases, females, and in 61 cases the sex was not mentioned. Thus the ratio of males to females was 1.5 to 1.

In 216 cases the patients were between 1 and 10 years of age; in 232 cases, between 11 and 20; in 231 cases, between 21 and 30; in 278 cases, between 31 and 40; in 297 cases, between 41 and 50; in 215 cases, between 51 and 60; in 93 cases, between 61 and 70, and in 18 cases, between 71 and 80. No case fell in the age group of 81 to 90 years; 1 was in the group of 91 to 100 and, finally, in 19 cases the age was not given.

In 905 cases the Babinski reflex was bilateral; in 682 cases it was unilateral, and in 13 cases no information as to the laterality was given. Thus the ratio of bilateral to unilateral recurrence was 1.3 to 1. Of the 1,600 cases, the Oppenheim reflex was reported to be present in 83; the Chaddock sign, in 65; the Hoffmann

sign, in 57; the Gordon sign, in 34; the Rossolimo sign, in 31; the Mendel-Bechterew sign, in 18, and the Schäffer sign, in 6, a total of 294 cases.

In 984 cases the knee jerk was reported as hyperactive; in 209 cases, as hypoactive, and in 32 cases, as normal, whereas in 375 cases it was not mentioned.

Ankle clonus was described as present in 400 cases, and the patellar clonus, in 70 cases.

Spasticity occurred in 548 cases, whereas flaccidity was characteristic in 87 cases.

Absence of abdominal reflexes was reported in 628 cases and absence of the cremasteric reflexes in 96 cases.

According to the descriptions, every degree of paralysis, when present, from slight to complete loss of the power of movement, goes hand in hand with the Babinski sign. In 51 cases the observers stated that they could not detect any somatic motor deficit on examination. In the great majority of cases, however, some degree of motor loss was present. In a number of cases the deficiency was confined to certain of the cranial muscles. Then, again, only muscles in the arm, or combinations of muscles of the head and arm, were paralyzed. In the lower extremities, voluntary motor deficit was classified by clinical investigators according to diminished strength in the muscles, to abnormalities in gait or to impaired movement. In some cases scientific terms were employed to designate loss of power of movement, such as hemiplegia, hemiparesis, paraplegia, paresis, palsy, tetraplegia or monoplegia, but such instances were in the minority.

Strength in the muscles was expressed by such terms as feebleness, weakness, impaired power, diminished power, weakness but no evident paralysis, fairly well preserved power, well preserved motor power and loss of power. Some of the terms used to express faulty gaits were dragging of the foot, inability to stand and walk, staggering, shuffling, unsteadiness, stumbling, slowness, sluggishness, limping, straddling and lameness. Expressions used to describe movement were motionlessness, slowness, awkwardness, clumsiness, feebleness and well preserved and limited movement.

Because there is evidence that suppression of nerve activity in the pyramidal tract alone or in combination with other tracts may be responsible for a potential Babinski sign, 199 cases were collected in which inhibition of somatic nerve activity was a possible factor. The disturbance was clinically classified as sleep, unconsciousness, coma, stupor, drowsiness and somnolence. In all (100 per cent) of 6 cases in which the patient was described as being in a state of sleep a bilateral Babinski sign was present. Corresponding values for the other states were as follows: unconsciousness, 35 of 39 cases (89.7 per cent); coma, 55 of 63 cases (87.3 per cent); stupor, 28 of 33 cases (84.8 per cent; drowsiness, 37 of 48 cases (77.0 per cent), and somnolence, 7 of 10 cases (70 per cent). The values for the entire series showed that in 168 of 199 cases, or 84.4 per cent, a bilateral Babinski sign was exhibited.

COMMENT

From the descriptions given in the reports of 1,600 cases with the Babinski sign, it is apparent that this reflex can be elicited in disease conditions in which the state of the voluntary striated muscles is judged to vary from normal to complete paralysis. In the majority of the cases there was some form of motor deficit, which, however, did not always involve the lower extremities. The motor loss was judged in terms of strength in the muscles, the appearance of the gait or the power of movement.

The seven pathologic reflexes other than the Babinski sign played an insignificant quantitative role in the 1,600 cases studied. Collectively, they were reported in only 294 cases (19.6 per cent).

The various pyramidal signs and symptoms which were reported can be graded with respect to their frequency in the following order: somatic motor deficit, 1,376 cases; hyperactive patellar reflex, 984 cases, absence of superficial abdominal reflexes, 628 cases; spasticity, 548 cases; ankle clonus, 400 cases; hypoactive knee jerk, 209 cases; absence of cremasteric reflexes, 96 cases; flaccidity, 87 cases, and patellar clonus, 70 cases.

In this series, the ratio of male to females involved was 1.5 to 1. Whether this distribution means that the motor system of the male is more susceptible to attack than that of the female is speculative.

Cases of the chronic type were more numerous than those of the acute form, the proportion being 2.1 to 1. The chronicity was determined for the series by the onset of motor difficulties. Thus, in all cases in which there was evidence of motor deficit of more than two months' duration the condition was classified as chronic.

The age factor in the series showed involvement in about an equal number of cases in each of the first six decades of life, and then there occurred a sharp fall between the seventh and

the tenth decade. The greatest actual number of cases was in the age groups of 41 to 50 years. One might expect the Babinski sign to be more prevalent in elderly persons, but it may be that not as many patients in the advanced age groups were examined.

An interesting feature of the study was the evaluation of the Babinski sign in cases in which unconsciousness, coma, stupor, sleep, drowsiness or somnolence was reported. These conditions clinically seem to simulate the states produced by hypoglycemic shock, loss of blood or the pharmacologic action of such drugs as pentobarbital, in which the Babinski sign can be elicited. In these neurologically suppressed conditions, a bilateral Babinski sign was common, occurring in 84.4 per cent of cases. In the entire series of 1,600 cases studied, the ratio of the incidence of a bilateral to that of a unilateral Babinski sign was 1.3 to 1. For the series of cases of coma, etc., the ratio was 5.4 to 1. The degree of general inhibition of nerve activity may be important, therefore, in the mechanism of the Babinski sign. It is possible that this reflex might have been elicited in 100 per cent of such cases had the attempt been made at a critical stage in the inhibitory process. The question arises: If general reduction of activity of the central nervous system can produce a state in which the Babinski sign may be elicited on stroking the outer portion of the sole, would local inhibition of the pyramidal tract without destruction do likewise? If the pyramidal bundle is concerned at all with the Babinski sign, I believe the latter may be a distinct possibility.

It is realized that the many clinicians who were involved in the present study did not select the majority of their cases for the purpose of investigating the pyramidal tract syndrome. The Babinski sign has been singled out in the literature in the form of individual cases and correlated with the signs and symptoms long regarded as being due to destruction of the pyramidal tract. Within the limits of the survey, there is an indication that the Babinski reflex goes hand in hand with all shades of muscular activity, from that judged to be normal to complete paralysis. Also, it is possible that an inhibitory factor may play a role in the mechanism of the Babinski reflex. In the absence of any extended investigations limited directly to the problem, it is believed that the over-all results of the study may indicate the true status of the Babinski sign in clinical medicine.

CONCLUSIONS

The results of a correlation study of 1,600 individual cases of the pyramidal tract syndrome in which the Babinski sign was exhibited may be summarized as follows:

1. The ratio of male to females was 1.5 to 1.
2. The Babinski sign occurred most frequently in the age group between 41 and 50 years and rapidly diminished in frequency after the sixth decade of life.
3. The proportion of cases of the bilateral Babinski sign to cases of the unilateral sign was 1.3 to 1.
4. Of about 200 selected cases in which were exhibited various degrees of general suppression of somatic nerve activity, such as that which occurs in sleep, unconsciousness, coma, stupor, drowsiness and somnolence, the Babinski sign was bilateral in about 85 per cent. The ratio of cases of the bilateral to cases of the unilateral Babinski sign in this group was 5.4 to 1.
5. All degrees of muscular activity, from the normal to complete paralysis, were judged to be present with the Babinski sign.
6. The signs and symptoms, in the order of their frequency, were as follows: somatic motor deficit, hyperactive patellar reflex, absence of superficial abdominal reflexes, spasticity, ankle clonus, hypoactive knee jerk, absence of cremasteric reflex, flaccidity and patellar clonus.
7. The criteria used to describe somatic motor deficit in the lower extremity were strength in the muscle groups, faultiness in gait and loss of power of movement.
8. Such pathologic reflexes as the Oppenheim, Chaddock, Hoffmann, Gordon, Rossolimo, Mendel-Bechterew and Schäffer signs played an insignificant quantitative role in the cases studied.

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PRIMITIVE HABITS AND PERCEPTUAL ALTERATIONS IN THE TERMINAL STAGE OF SCHIZOPHRENIA

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In the last decade the main interest in the study of schizophrenia has been concentrated on cases of the early stage of this illness, which are the most suitable for dynamic psychologic investigations and in which a better response to the newly devised shock treatments is obtained. The study of cases of chronic schizophrenia has, on the other hand, been rather neglected except for statistical purposes. I am in accord with the numerous other workers who think that even the study of patients in the most advanced stages of this illness may eventually reveal important information on the nature of this condition. This point of view led to the present investigation of peculiar habits and of quasineurologic (or neurologic?) phenomena noted in the terminal stages of dementia precox. The word habit is employed here for want of a better term. It is used to mean a certain type of behavior intermediate between reflexes and voluntary acts but always definitely reactive in nature. Goldstein's [1] term "performance" could be used except for the fact that the behavior discussed here is a special kind of performance, being spontaneous and habitual. The term "automatic act" is also discarded because by this term is often meant an act which has become such through repetition or training. The study on the coprophagic habit has already been reported.[2] The habit of "placing into mouth" has also been discussed [2] but will be reconsidered here in relation to broader implications. The phenomenon of negativism will not be included in this report because it is not found exclusively in the terminal stage of dementia precox but is more characteristic of less advanced stages. Other habits which belong to preterminal stages of dementia precox will be discussed in later contributions.

This study was carried out on 250 female patients with the chronic form of schizophrenia who had been hospitalized in institutions for mental disease from seven to forty-seven years.

From the New York State Psychiatric Institute and Hospital and Pilgrim State Hospital.

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OBSERVATIONS

It is well known to all observers that decreased activity is one of the most common, though not a constant, characteristic of progressing schizophrenia. This motor reduction often interferes with the dietary requirements of the patient to such a point as to bring about a state of malnutrition, anemia and, occasionally, avitaminosis. This inactivity, which is a part of the psychic isolation of schizophrenia, is noted throughout the long years of progressing regression, interrupted only by occasional and transitory partial remissions. In patients, however, who continue to regress indefinitely, a more or less sudden increase in motor activity is noted at a certain moment. As a rule such an increase is not transitory but lasts for the lifetime of the patient, or until a physical illness neutralizes its effects. It is when this partial increase of motor activity takes place that what I call the terminal stage of dementia precox begins. In the patients whom I observed and whose clinical records I studied, such a stage started any time from seven to forty years after the onset of the illness, but it probably may start even sooner, or later. This increase in activity is only relative, since the patients remain somehow underactive in comparison with normal subjects. Their actions, which are now more numerous, appear sharply reactive or impulsive: They are reactive to certain habitual situations, which will be taken in consideration shortly, or impulsive, inasmuch as they appear to be due to sudden internal stimulation. The patients may be impulsively destructive, assaultive and much more violent than previously. At this stage of the illness they do not seem able any longer to experience hallucinations or to elaborate delusions, although it may be that since they are no longer capable of expressing themselves verbally, such symptoms cannot be elicited. In fact, their verbal expressions are either completely absent or reduced to a few disconnected utterances.

The most striking changes, however, are noted in the dining room. The patients who had

always eaten so little as to have reduced themselves to a state of malnutrition now seem to have a voracious appetite (bulimia) and often gain a considerable amount of weight. The nurses often report that these patients have the habit of stealing food. In reality, closer observation reveals that the concept of stealing is not implied in the actions of these patients. They cannot prevent themselves from grabbing food at the sight of it, so that they are better termed food grabbers. Observations in the dining room reveal other interesting habits. A few of these patients show preference for certain foods. No matter how many kinds of food are in their dish, they always grasp first and eat the preferred food. They do not alternate the various kinds, as normal adults do, but only when they have entirely finished the preferred food do they start to eat the others. Similarly, if they show several degrees of preference, they first eat the food which is the first choice; when this is finished, they eat the second choice, and so on. If there are desserts, they are generally eaten before anything else. It seems that the patients are obliged to react first to stronger stimuli. The preference for a certain food is not shown by all patients who are food grabbers. On the other hand, such preference is maintained only for a brief period after the acquisition of the food-grabbing habit. After this period the patients seem to eat with avidity any kind of food. Whatever belongs to the category of edibility is equally and promptly reacted to. Another characteristic which is often observed is the extreme rapidity with which these patients eat (tachyphagia). In a few minutes these food grabbers may finish the rations of several patients, if not prevented. Often they do not leave in the dish any remnant of food but clean the plate with their tongue.

The patients may remain indefinitely at this stage characterized by the food-grabbing habit, but the majority progress more or less rapidly to a more advanced stage, characterized chiefly by what I have termed the habit of "placing into mouth." At this stage the category of edibility is no longer respected. Whereas the patients had previously distinguished themselves for grabbing food and food only, now they manifest the habit of grabbing every small object and putting it into the mouth, paying no attention at all to the edible or nonedible nature of it. If not prevented, these patients pick up from the floor crumbs, cockroaches, stones, rags, paper, wood, clothes, pencils and leaves and put them into the mouth. Generally they eat these things; occasionally they swallow them, with great risk. Many patients, however, limit themselves to chewing these nonedible objects and finally reject them. When they eat or swallow dangerous materials, such as an ink well or a teaspoon, they are erroneously considered as suicidal. Closer observation reveals, however, that the idea of suicide is not implied in their action. They simply react to a visual stimulus by grasping the object and putting it into the mouth. They act as if they were coerced to react in this way. It is as though they were especially attracted by small three dimensional stimuli, which seem to be distinguished more distinctly than usual from the background.

The patient may remain indefinitely at this stage, but some of them progress to a more advanced phase, which is characterized by apparent sensory alterations. On account of the lack of cooperation and communicability of these patients, such alterations cannot be studied with the usual neurologic technic, but much stronger stimuli, not ordinarily used, or observation of the patient's reactions in certain special situations must be employed. Therefore only gross alterations are reported here, and no claim to accuracy is made.

It seems as though the patients who have reached this stage are insensitive to pain. They appear analgesic not only to pinprick but to much more painful stimuli. When they are in need of surgical intervention and have to have sutures in such sensitive regions as the lips, face, skull or hands, they act as though they could not feel anything, even in the absence of any anesthetic procedure. I have many times sutured wounds caused by their violent and assaultive behavior without eliciting any sign of pain or resistance. Other patients seem to feel some pain, but far less than normal persons would. Only exceptionally is there a local withdrawal. The same anesthesia is noted for temperature. The patient may hold in his hands a piece of ice without showing any reaction. Pieces of ice may also be placed over the breast, abdomen or other sensitive regions without eliciting any reaction or defensive movement. Such patients also appear insensitive when the flame of a candle is passed rapidly over the skin. They may sit near the radiator, and if they are not removed, they may continue to stay there even when, as a result of close contact, they are burned. This state of insensitivity is in my opinion one of the chief causes of the large number of burns occurring in wards in which deteriorated schizophrenic patients live.

One may be induced to interpret this lack of responsiveness to pain and temperature stimuli not as true anesthesia but as an expression either of catatonic inactivity or of a certain kind of "inner negativism." Repeated observations have,

however, led me to the conclusion that such an interpretation is not valid. The patients who show anesthesia for pain or temperature stimuli are not as a rule inactive; on the other hand, they show the aforementioned relative increase in activity which, together with the apparent anesthesia, is responsible for numerous accidents. The possibility that these patients do not react to dangerous sensations on account of inner negativism is, in my opinion, also untenable because many such patients do not show other signs of negativism. As I have already mentioned, the phenomenon of negativism, although not absent at this stage of the illness, is much more commonly observed in patients who have reached a less advanced stage. On the other hand, the possibility that pain and temperature sensations are perceived, but that only the affective components of such perceptions are lost, must be taken into consideration and will be discussed later. In a small number of patients this apparent anesthesia or hypesthesia for pain and temperature stimuli is only transitory. Even patients who have been insensitive to heat for several months may to some extent reacquire capacity to perceive pain or temperature sensations or both. Occasionally striking changes occur at brief intervals. However, I have the impression that some degree of hypesthesia is always retained. Partial hypesthesia is also found in many patients who have not yet reached what is here called the terminal stage. Tactile perception does not seem impaired in these patients. Tendon and superficial reflexes are not only present but often increased. The corneal reflexes are also present. On the other hand, many, but not all of the patients who present anesthesia for pain and temperature stimuli seem also to have lost the sensation of taste. When they are given bitter radishes or teaspoons of sugar, salt, pepper or quinine, they do not show any pleasant or unpleasant reaction. They do not spit out the unpleasant substances as quickly as possible, as do control mentally defective persons or deteriorated patients with organic disease, but continue to eat the entire dose without hesitation. Some of them seem to recognize salt but do not object to pepper or quinine. Others react mildly to quinine but not to pepper or salt.

In contrast to this lack of reactivity to pain, temperature and taste stimuli is the normal reaction to strong olfactory stimuli. Patients who did not react at all to such stimuli as flames, pieces of ice and suturing react in a normal way when they smell such things as ammonia and strong vinegar. They withdraw quickly from the stimulus, with manifest displeasure. Such a reaction strikes the observer, inasmuch as many other strong stimuli from other sensory fields do not bring about any response, or only a mild reaction. It seems as though the phylogenetically ancient olfactory sense could better resist the schizophrenic process. However, the schizophrenic patient does not seem to make use of these olfactory sensations as he could, probably on account of that lack of initiative which more or less characterizes the entire course of his illness.

The aforementioned phases of the terminal stage of dementia precox (phases characterized by the food-grabbing habit, the "placing into mouth" habit and apparent anesthesia for pain, temperature and taste sensations and preponderance of the olfactory sense, respectively) do not always occur in the order given. A large number of patients, especially, but not exclusively, those of the paranoid type, remain indefinitely at a less advanced stage. In others two stages of the illness overlap. For instance, a few patients who have the food-grabbing habit may retain the capacity to hallucinate. Other food grabbers may already have anesthesia for pain and temperature stimuli, and so on. However, the order described is the one in which I have most commonly observed appearance of the symptoms. Occasionally a patient may improve and return to a less advanced stage. Intravenous injections of sodium amytal do not produce any perceptible change in the picture of the terminal stage of schizophrenia.

Although statistical conclusions are premature and difficult on account of this overlapping of symptoms, I have the impression that the number of patients presenting the habit of grabbing food or of placing objects in the mouth is large in services for patients with chronic mental disease. The number of patients presenting some hypesthesia for pain, temperature and taste sensations is also large. On the contrary, patients presenting absolute anesthesia for pain and temperature sensations are relatively few.

INTERPRETATION

A genetic approach may help in explaining some of the habits described. In fact, it is possible to interpret them not as newly acquired habits but as behavior manifestations of lower levels of integration.

The food-grabbing habit reminds one of what is generally observed in cats, dogs, monkeys and other animals. The animal is coerced to react to the food, at the sight of it. The food does not stand for itself but is what Werner [3] calls

3. Werner, H.: Comparative Psychology of Mental Development, New York, Harper & Brothers, 1940.

a "thing of action." It is a "signal thing," the sight of which leads immediately to a fixed action (Werner [3]). The animal cannot delay the reaction or channel the impulse into longer integrative circuits. Similarly, others of the habits previously described disclosed the same syncretic characteristics encountered in more primitive organizations. It is well known that when monkeys, dogs, cats and other animals are given at the same time different items of food, they eat first the preferred food (for instance, meat in case of the dog, or banana in case of monkeys), and only when the entire portion of the preferred food is finished do they start to eat the other foods. They cannot alternate the various kinds but are coerced to react first to the strongest stimulus. Also, a 3½ to 4 year old child, if not prevented, eats first the preferred food, and only when he has finished it does he eat the others.

When the patients become even sicker, this integration of the stimuli is even more primitive, so that they react to edible and nonedible objects in the same way by grasping them and putting them into the mouth. The category of edibility is no longer respected. This "placing into mouth" habit was discussed in a previous report.[2] It was there emphasized that a similar behavior is noted in children approximately 1 to 2 years of age. The similarity of this behavior to that observed by Klüver and Bucy [4] in monkeys which underwent removal of both temporal lobes was also discussed. There is one chief difference, however: Whereas the monkeys are described as smelling the grasped object before placing it into the mouth, children and deteriorated schizophrenic patients do not smell the object but put it immediately into the mouth. However, if the olfactory tracts of the monkeys were cut previous to removing both temporal lobes, no smelling was observed. Klüver and Bucy considered the monkeys with both temporal lobes removed as psychically blind (being unable to recognize the edible or nonedible nature of the objects in spite of the fact that they were trained before the operation to make this differentiation). I am inclined to consider the "placing into mouth" habit in deteriorated schizophrenic patients as a primitive response in the mechanism of which a short-circuiting takes place between the functions of reception and those of reaction, with exclusion of usual normal paths which involve higher centers. It may be that instead of the normal path a circuit is used similar to that involved in the relatively primitive physiologic complex which Edinger [5] called "oral sense." As happens in all other short-circuit reactions, an impulse or coercion to react, and not asymbolia, may be responsible for the "placing into mouth" habit. Klüver and Bucy considered as hopeless any attempt to reduce to one basic defect the polysymptomatic picture presented by their monkeys with bitemporal lobectomy. Although any comparison is hypothetic, it may be that these monkeys have this oral habit because after the surgical operation they are coerced to react to tridemensional visual stimuli and have to use short circuits. This consideration, however, does not deny the possibility that these monkeys are, at least partially, psychically blind. On the other hand, they probably are psychically blind, as considerations to be discussed later will indicate. The same inability to distinguish between edible and nonedible objects was also noted by Langworthy [6] in cats which underwent removal of both frontal poles. The tendency to grasp every object and to put it into the mouth was also reported by von Braunmühl and Leonhard [7] in cases of Pick's disease. It may be of some importance to mention also that I have noted the sudden occurrence of bulimia, tachyphagia and the "placing in mouth" habit after bilateral prefrontal lobectomy in a catatonic patient who had been sick for more than ten years.

The analgesia observed in some of the deteriorated patients may now be considered. Several authors have reported altered perception of pain in cases of early catatonia, and Bender and Schilder [8] discussed this subject in relation to the capacity to acquire conditioned reflexes. In my experience the hypesthesia found in patients with early catatonia is generally not so severe as that observed in patients who have reached the terminal stage, and often is not detected if, instead of pinprick, one uses stronger stimuli. Anesthesia for temperature and taste

4. Klüver, H., and Bucy, P. C.: (*a*) "Psychic Blindness" and Other Symptoms Following Bilateral Temporal Lobectomy in Rhesus Monkeys, Am. J. Physiol. **119**:352 (June) 1937; (*b*) An Analysis of Certain Effects of Bilateral Temporal Lobectomy in the Rhesus Monkey, with Special Reference to "Psychic Blindness," J. Psychol. **5**:33, 1938; (*c*) Preliminary Analysis of Functions of the Temporal Lobes in Monkeys, Arch. Neurol. & Psychiat. **42**:972 (Dec.) 1939.

5. Edinger, L.: Ueber die dem Oralsinne dienenden Apparate am Gehirn der Säuger, Deutsche Ztschr. f. Nervenh. **36**:151, 1908-1909.

6. Langworthy, O. R.: Behavior Disturbances Related to Decomposition of Reflex Activity Caused by Cerebral Injury: An Experimental Study of the Cat, J. Neuropath. & Exper. Neurol. **3**:87 (Jan.) 1944.

7. von Braunmühl, A., and Leonhard, K.: Ueber ein Schwesternpaar mit Pickscher Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **150**:209-241, 1934; cited by Klüver and Bucy.[4c]

8. Bender, L., and Schilder, P.: Unconditioned and Conditioned Reactions to Pain in Schizophrenia, Am. J. Psychiat. **10**:365 (Nov.) 1930.

stimuli is even more rare in patients with early catatonia and is not comparable to that encountered in my patients, with conditions originally diagnosed as various types of dementia precox. However, the possibility is not denied that the nature of the phenomenon may be the same. In many of the common textbooks on psychiatry no mention is made of this analgesia encountered in some deteriorated schizophrenic patients. Bleuler,[9] however, described this phenomenon as follows:

> Worthy of note is an analgesia which occurs in schizophrenia not too rarely and which is sometimes quite complete. It is responsible for the fact that the patients readily injure themselves purposely or accidentally.

In agreement with the observations of Bender and Schilder on patients with early catatonia, I am inclined to believe that the real sensation of pain and temperature is not lost in my patients. The fact that the corneal reflexes are always retained may be a proof of it. However, these patients seem to be unaware of the painful and thermic stimuli and do not show any emotional reaction to them. They seem to be unable to perceive the stimuli. In other words, the rough sensation may be present but remains isolated and is not elaborated to the perception level. The patients are unable to recognize the emotional and cognitive value of the thermic and painful stimuli and therefore are unaware of the possible dangers which they at times imply. That is the reason that they often hurt themselves. These patients for all practical purposes have agnosia and may be compared to persons with sensorial aphasia who hear a spoken language without understanding it.

Is this loss of nociceptive perception only an exaggeration of the general schizophrenic emotional indifference? Probably the cause of these psychophysiologic derangements is the same, but for all practical purposes these patients are better described as having agnosia and may be termed "psychically analgesic," and not apathetic only. They fail to perceive pain and temperature sensation, not only from an emotional but from a cognitive point of view. That is the reason that they so often hurt themselves if they are not under constant supervision. The problem whether these phenomena are due to loss of emotional capacity or to loss of perception of pain and temperature sensation is probably only academic at present, when so little is known about emotivity and its relation to perception of pleasant and painful sensations. Herrick,[10] who took into consideration this relation, stated: "Pain, considered psychologically and neurologically, is a sensation, and a different neurological mechanism for unpleasantness and pleasantness must be sought." Pain, however, is in normal conditions always associated with unpleasantness. In the patients described it is not. The relation between emotional indifference and agnosia has also been taken into consideration by von Monakow and Mourgue,[11] who observed impairment of emotions in aphasic persons. In other publications[12] the same authors considered the possibility that asymbolia may be due to disturbances in the affective sphere.

The fact that taste perception is often lost or impaired in these analgesic patients and that the olfactory perceptions are preserved instead is also thought stimulating. The association of taste and pain asymbolias points to the conclusion that taste should be included among the general somatic sensations, as investigations by the school of Fulton[13] and by Shenkin and Lewey[14] seem to prove. The striking survival of smell perceptions, which are phylogenetically very old, may induce one to think that the archipallium is more resistant than the neopallium to the schizophrenic process. The olfactory sense, which is the dominant sense in lower vertebrates, seems to reacquire in some deteriorated schizophrenic patients a position of predominance among the senses, not because of increased acuity but because of impairment of perceptions of stimuli coming from other sensory

9. Bleuler, E.: Textbook of Psychiatry, translated by A. A. Brill, New York, The Macmillan Company, 1924.

10. Herrick, C. J.: An Introduction to Neurology, ed. 5, Philadelphia, W. B. Saunders Company, 1931.

11. von Monakow, C. V., and Mourgue, R.: Introduction biologique à l'étude de la neurologie et de la psychopathologie, Paris, Félix Alcan, 1928.

12. von Monakow, C. V.: Die Lokalisation in Grosshirn und der Abbau der Funktionen durch korticale Herde, Wiesbaden, J. F. Bergmann, 1914. Mourgue, R.: Neurobiologie de l'hallucination: Essai sur une variété particulière de désintégration de la fonction, Brussels, Maurice Lamertin, 1932; cited by Klüver and Bucy.[4c]

13. The following works are cited by Fulton, J. F.: Physiology of the Nervous System, ed. 5, New York, Oxford University Press, 1943. (*a*) Börnstein, W. S.: Cortical Representation of Taste in Man and Monkey: I. Functional and Anatomical Relations of Taste, Olfaction and Somatic Sensibility, Yale J. Biol. & Med. **12**: 719 (July) 1940; (*b*) II. The Localization of the Cortical Taste Area in Man and a Method for Measuring Impairment of Taste in Man, ibid. **13**:133 (Oct.) 1940. (*c*) Patton, H. O., and Ruch, T. C.: Thalamic and Cortical Localization of Taste in Monkey and Chimpanzee, to be published.

14. Shenkin, H. A., and Lewey, F. H.: Taste Aura Preceding Convulsions in a Lesion of the Parietal Operculum, J. Nerv. & Ment. Dis. **100**:352 (Oct.) 1944.

fields. However, contrary to what is found in lower vertebrates, these schizophrenic patients do not take advantage of the olfactory sense as they could, possibly on account of their general volitional impairment or general withdrawal. It is interesting to observe that the sense of smell in schizophrenic patients is not involved even in short-circuiting reactions, whereas it was involved in the monkeys of Klüver and Bucy. The fact that perception and emotional reactions connected with the sense of smell are not impaired in many patients in the terminal phases of schizophrenia may be due instead to the peculiarity that the olfactory stimuli are the only sensory stimuli which do not pass up to the thalamus.

The last consideration may induce one to examine the possibility of anatomic interpretations of the symptoms described. Any interpretation of this kind has of course to be considered preliminary at the present time, when so much remains to be learned about the schizophrenic process. Furthermore, any deduction concerning human beings made from experimental observations on animals may be advanced only in a hypothetic way.

If, on the basis of reported observations, one were to localize an alleged pathologic process responsible for the release of the primitive habits previously described, one would probably have to incriminate the prefrontal lobes (Langworthy) and the temporal lobes, (Klüver and Bucy, von Braunmühl and Leonhard), and the lesions would have to be bilateral and presumably symmetric. The problem of localizing the process responsible for the analgesia is even more difficult, after the work of Head, although there is again much evidence that the parietal lobes are the site of sensation and perception of pain. Schilder and Stengel [15] found asymbolia for pain in cases of lesions of the gyrus supramarginalis; Bender and Schilder expressed the belief that it is impossible to deny the presence of a dysfunction of the same areas in catatonic patients presenting pain asymbolia. Patterson and Stengel [16] reported "apperceptive blindness" and asymbolia for pain in a case of Lissauer's dementia paralytica in which lesions in the parastriatal areas were present. Since in my patients pain asymbolia is often associated with taste asymbolia, or "psychic ageusia," it may be that the perceptual centers for taste and pain are located near each other. It has already been mentioned that recent investigations seem to confirm a parietal localization of the taste centers.[17] These anatomic considerations are not solidly founded. However, one deduction has a certain probability of being correct. If, on the basis of the reported observations, one were to localize an alleged pathologic process responsible for the symptoms occurring in the terminal stage of schizophrenia, one would have to place it in the so-called silent areas, or great association areas, and not in the recognized primary cortical centers. These areas would, also, be approximately those which, according to the investigations of Flechsig [18] and Vogt,[19] are the last to myelinate and the last to appear phylogenetically. Bilateral impairment of these great association areas would make impossible those "long-circuiting processes" mentioned by Fulton [20] and reemphasized by Cobb,[21] and would be responsible for the occurrence of short-circuit processes manifesting themselves as primitive habits.

The theories of Orton [22] seem also confirmed by my observations. According to this author, three levels of cortical elaborations may be distinguished.[22a] The first elaborative level, consisting of the so-called projection areas, or the arrival platform cortex, is the first to receive stimuli of external origin. The second level, consisting of the areas surrounding the projection zones, or the arrival platform cortex, registers and interprets the material arrived at the first level. The third level, consisting of the great associative areas, which are the last to myelinate, correlates the data brought in by the various pathways. According to Orton, impairment of a level causes "cross over" of impulses from a lower level to the effectors, so that primitive patterns of reactions are produced. He called this return of primitive patterns "resurgence by defect." [22b] Orton stated the opinion that in catatonia there is an impairment of the third level of elaboration.[22a] In extremely deteriorated schizophrenic patients one may assume that the

15. Schilder, P., and Stengel, E.: Asymbolia for Pain, Arch. Neurol. & Psychiat. **25**:598 (March) 1931.

16. Patterson, M. T., and Stengel, E.: Apperceptive Blindness in Lissauer's Dementia Paralytica, J. Neurol. & Psychiat. **6**:83 (July) 1943.

17. Footnote 13. Shenkin and Lewey.[14]

18. Flechsig, P.: Ueber die Lokalisation der geistigen Vorgange insbesondere der Sinnesemfindungen des Menschen, Leipzig, Veit & Co., 1896.

19. Vogt, O.: Der Wert der myelogenetischen Felder der Grosshirnrinde, Anat. Anz. **29**:273, 1906.

20. Fulton, J. F.: Physiology of the Nervous System, ed. 4, New York, Oxford University Press, 1938; cited by Cobb.[21]

21. Cobb, S.: Foundations of Neuropsychiatry, Baltimore, Williams & Wilkins Company, 1941.

22. Orton, S. T.: (*a*) The Three Levels of Cortical Elaboration in Relation to Certain Psychiatric Symptoms, Am. J. Psychiat. **8**:647 (Jan.) 1929; (*b*) Neuropathology: Lecture Notes, Arch. Neurol. & Psychiat. **15**:763 (June) 1926; (*c*) Some Neurologic Concepts Applied to Catatonia, ibid. **23**:116 (Jan.) 1930.

third, and partially the second, level of elaboration are impaired. In this way it is possible to explain both certain asymbolias and the short-circuiting processes which resurge by defect. It is now also possible to understand better the complex symptoms reported in the valuable contributions of Klüver and Bucy. The monkeys deprived of both temporal lobes also present visual asymbolia and primitive habits ("placing into mouth" or "oral tendency"). Since the great association areas have undoubtedly thalamic connections (Ariëns Kappers and associates [23]), it may be possible to find an anatomic interpretation of the emotional impairment.

All the foreging evidence suggests, but does not demonstrate, that the schizophrenic process either is organic in nature or at a certain stage is associated with organic changes. Goldstein's [24] position when he stated "I am inclined to assume that equivalent functional changes can be produced by organic, i. e., structural or clinical as well as by psychological derangement" may be maintained. He spoke also of "protective deterioration," after having described certain similarities between the impairment of abstract thinking associated with schizophrenia and that accompanying organic lesions.

The new phychosomatic concepts may also be resorted to. If Weiss and English's [25] formula, "psychologic disturbances → functional impairment → cellular disease → structural alteration," is accepted to explain the pathogenic mechanisms of cardiovascular and gastrointestinal conditions, why should it not be accepted to explain derangement of the nervous system, which is more directly under the fire of psychologic stimuli? The functions or structures which are phylogenetically more recent may be the ones more easily impaired, even by psychologic stimuli, so that when, after a long course, the impairment is complete or almost complete, resemblance may be obtained to lower levels of integration which have not yet acquired such functions or structures. Thus, the terms "regression" and "deterioration" would have the same meaning when applied to schizophrenic patients, unless by deterioration one wants to specify only the irreversibility of the syndrome; and for both may be substituted Lewis' [26] term "deviation."

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23. Ariëns Kappers, C. U.; Huber, G. C., and Crosby, E. C.: The Comparative Anatomy of the Nervous System of Vertebrates, Including Man, New York, The Macmillan Company, 1936, vol. 2.

24. Goldstein, K.: The Significance of Psychological Research in Schizophrenia, J. Nerv. & Ment. Dis. **97:** 261 (March) 1943.

25. Weiss, E., and English, O. S.: Psychosomatic Medicine: The Clinical Application of Psychopathology to General Medical Problems, Philadelphia, W. B. Saunders Company, 1943.

26. Lewis, N. D. C.: Personal communication to the author.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

VASOPRESSOR AND CAROTID SINUS SYNCOPE: CLINICAL, ELECTROENCEPHALOGRAPHIC AND ELECTROCARDIOGRAPHIC OBSERVATIONS. GEORGE L. ENGEL, JOHN ROMANO and T. R. MCLIN, Arch. Int. Med. **74**:100 (Aug.) 1944.

Engel, Romano and McLin report clinical, electroencephalographic and electrocardiographic observations on 18 persons subjected to syncope. Most of the subjects were examined on a tilt table. Before any special syncope-provoking procedure was attempted, the reaction to motionless standing for at least ten minutes was tested. The special procedures were initiated when it was clear that the postural response was normal. Reactions to syncope followed venipuncture, visceral distention, hyperventilation and stimulation of the carotid sinus, or they were associated with hypersensitivity of the carotid sinus reflex. The blood pressure was recorded as frequently as was practical, and continuous observations were made on the color of the skin, sweating, subjective responses and other changes.

Vasodepressor syncope was induced in 9 subjects by one of the aforementioned procedures. In addition, 6 subjects with the cardioinhibitory type of carotid sinus syncope and 3 subjects with the cerebral type were studied.

Unconsciousness, characterized by unawareness, muscular relaxation and falling, was always accompanied with high voltage slow waves in the electroencephalogram, regardless of the mechanism by which unconsciousness was provoked. Lightheadedness, giddiness and momentary loss of consciousness were associated with less obvious slowing of the electroencephalogram, loss of alpha activity or no change at all. In 2 subjects with the cerebral type of carotid sinus syncope the development of contralateral focal neurologic symptoms and signs without loss of consciousness was associated with abnormal waves from the ipsilateral cortex.

Vasodepressor syncope could be provoked by a wide variety of sensory stimuli, but the significance of the stimulus to the subject seemed to be more important than the specific modality involved. Most of the symptoms of vasodepressor syncope were associated with falling arterial blood pressure, and unconsciousness did not develop until the blood pressure had fallen to a low level. Symptoms were relieved by returning the subject to the recumbent position, but they often recurred if the subject stood up again, even if the original stimulus had been withdrawn. The derangement in circulatory dynamics was compensated for but not corrected by assumption of the recumbent position, presumably by avoiding the pooling effects of gravity. Recovery of consciousness may occur in the erect position; convulsive moments and increase in muscle tone seemed to aid recovery, but they were not essential. Muscular activity prior to assumption of an erect position prevents recurrence of syncope.

GUTTMAN, Philadelphia.

EXPERIMENTAL ANALYSIS OF THE FUNCTIONS OF THE BASAL GANGLIA IN MONKEYS AND CHIMPANZEES. MARGARET A. KENNARD, J. Neurophysiol. **7**:127 (March) 1944.

Kennard studied in monkeys and chimpanzees the effects of destruction by various routes of the different parts of the basal ganglia. She found that lesions of one or more of the nuclear complexes of the basal ganglia produced disorders of movement similar to the choreoathetosis and tremor seen in patients with involvement of these same regions. Choreiform movements appeared to any marked degree only in chimpanzees but developed in slight form in monkeys. The disturbances were always contralateral to the ablation, were transient and affected the arm and head more than the leg. Tremor, which was absent during complete rest but was present on movement or maintenance of posture, occurred in both chimpanzees and monkeys and was bilateral. Kennard concludes that two systems are present within the basal ganglia, yielding choreoathetosis and tremor respectively, and that these systems do not greatly influence each other nor can they be topographically distinguished. Kennard states that the relation of spasticity or rigidity to the basal ganglia has not been clarified but that isolated lesions of the basal ganglia in her animals did not alter resistance to passive manipulation. The addition of corticosubcortical lesions to pure cortical ablations augmented the increased resistance. Moreover, the removal of the basal ganglia after decortication increased the resistance which had followed decortication. The difference in results obtained in monkeys and in chimpanzees was associated with changes in the putamen and the extrapyramidal cerebral cortex and with the development of manual dexterity.

FORSTER, Philadelphia.

THE HIND BRAIN AND THE EARLY DEVELOPMENT OF BEHAVIOR IN FROGS. GING-HSI WANG and TSE-WEI LU, J. Neurophysiol. **7**:151 (May) 1944.

Wang and Lu studied the responses of tadpoles to tactile stimulation, both during their normal developmental states and after decapitation, transection of the neural axis at various levels and removal of one ear vesicle. Studies were also carried out on parabiotic twins, one of the pair being decapitated; and observations were made on normal, as well as on decapitated, tadpoles after immersion in solutions of potassium cyanide. Wang and Lu found that the duration of the tactile reflex decreased with increase in size of the tadpole. Decerebration or section of the dorsal portion of the cord had no effect on the duration of the reflex. Destruction of the rostral half of the hindbrain or transection of the surgical cord had no effect in embryos of 3 mm. length, but in larvae longer than 4 mm. the duration of the reflex was increased by these measures. During the early stages of cyanide poisoning the duration of the reflex was increased both in normal and in decerebrate preparations but was not affected in spinal and bulbospinal preparations. Spinal tadpoles were more active than normal or decerebrate larvae. Cyanide poisoning in its earlier stages increased the

spontaneous activity of normal and decerebrate tadpoles. Wang and Lu conclude that a mechanism is laid down in the cord of the tadpole for repeated reactions to brief tactile stimuli and that this mechanism is inhibited by impulses from the rostral half of the hindbrain. In an appendix, the authors point out that cyanide depresses the developing, as well as the adult, nervous system of the frog and that the last structure to mature is the first to succumb. Susceptibility to cyanide increases with the age of the embryo.

FORSTER, Philadelphia.

EXPERIMENTAL HYPOGEUSIA FROM HORSLEY-CLARKE LESIONS OF THE THALAMUS IN MACAÇA MULATTA. H. D. PATTON, T. C. RUCH and A. E. WALKER, J. Neurophysiol. **7**:171 (May) 1944.

Patton, Ruch and Walker studied the capacity for gustatory discrimination for quinine hydrochloride in 10 immature Macaca mulatta monkeys before and after the production of bilateral electrolytic lesions of the posteroventral lateral nucleus of the thalamus. The lesions were produced under aseptic conditions and by means of the Horsley-Clarke apparatus. The authors found that the degree of damage to the posterolateral ventral nuclei as determined by microscopic examination could be correlated with the severity of the gustatory deficit. On the basis of these observations, the authors conclude that the evidence supports the hypothesis that taste fibers synapse in close association with fibers bearing somatosensory impulses from the face, mouth and tongue. Since the posterolateral ventral nucleus has no known connecting pathways with the uncus and hippocampal region and since this nucleus degenerates as a result of lesions of the sensory area for the face, Patton, Ruch and Walker conclude that their observations are in conformity with the hypothesis that taste is localized in the inferior portion of the rolandic area.

FORSTER, Philadelphia.

PHYSIOLOGICAL NEURONOGRAPHY OF SOME CORTICO-SUBCORTICAL CONNECTIONS IN THE CHIMPANZEE. H. W. GAROL and W. S. MCCULLOCH, J. Neurophysiol. **7**:199 (May) 1944.

Garol and McCulloch studied cortical connections in 7 chimpanzees under dial anesthesia, placing electrodes over the cortical surface and intracerebrally. By means of strychnine firing, the authors mapped the cortico-subcortical neuronal connections. They succeeded in demonstrating the following connections: (1) a cortico-caudate system from areas 8, 4s, 2 and 24; (2) a cortico-putamen system from areas 6, 4 and 1; (3) a corti-copallidal system to the external segment from area 6 and to the internal segment from what were questionably areas 4 and 5; (4) a corticopulvinar system from areas 40 and 39; (5) a corticothalamic connection from the arm subdivision of the central sector to the corresponding portion of the lateral thalamic nucleus.

FORSTER, Philadelphia.

THE ISOLATION OF THE ST. LOUIS ENCEPHALITIS VIRUS FROM CHICKEN MITES (DERMANYSSUS GALLINAE) IN NATURE. MARGARET G. SMITH, RUSSEL J. BLATTNER and FLORENCE M. HEYS, Science **100**:362 (Oct. 20) 1944.

Smith, Blattner and Heys report data which show that the St. Louis encephalitis virus is present in chicken mites (Dermanyssus gallinae) taken directly from chickens. These observations were made in the St. Louis area during a nonepidemic period. Other investigators have previously shown that the mosquito is a vector concerned in human epidemics of St. Louis encephalitis.

GUTTMAN, Philadelphia.

AFFERENT AREAS IN THE CEREBELLUM CONNECTED WITH THE LIMBS. E. D. ADRIAN, Brain **66**:289, 1944.

Adrian studied the electrical activity of the cerebellar cortex and the cerebellar subcortical afferent fibers in monkeys and cats. In a few instances electrical stimulation was used, but in most experiments mechanical stimulation of the skin, joints and muscles was employed.

Afferent discharges reaching the cerebellum by spinocerebellar and pontocerebellar pathways were recorded from a depth of 1.5 mm. below the cerebellar cortex. With this method it was possible to make a detailed map of connections. In both cat and monkey spinocerebellar discharges from the hindbrain arrive in the ipsilateral lobulus centralis, and those from the forelimb, in the culmen. Records of the afferent discharge in single units differ little from records of peripheral nerve fibers. A single afferent unit of the cerebellum may be connected with widely separated receptor organs. Pontocerebellar discharges to the lobulus centralis, the culmen and the lobulus simplex are derived from the hindlimb, the forelimb and the face region of the motor cortex. The receiving areas in these structures overlap those of the spinocerebellar pathway but extend farther laterally than the latter. The electrical activity of the cerebellar cortex consists of small potential waves of 150 to 250 per second, and afferent discharges result in increase of both frequency and amplitude. This effect tends to spread. In 2 dogs and 1 goat similar localizations were made. Adrian points out that the arrangement for afferent localizations is the opposite of that deduced for efferent localization by Connor and Graham.

FORSTER, Philadelphia.

POLIOMYELITIS IN BRITISH AND AMERICAN TROOPS IN THE MIDDLE EAST: THE ISOLATION OF VIRUS FROM HUMAN FAECES. J. R. PAUL, W. P. HAVENS and C. E. VAN ROOYEN, Brit. M. J. **1**:841 (June 24) 1944.

Attempts were made to isolate the virus of poliomyelitis from the stools in 35 cases of typical and atypical poliomyelitis which occurred during 1943 among British and American troops stationed in the Middle East. The following clinical types were studied: typical poliomyelitis, 15 cases; polioencephalitis with a short febrile course and paralysis limited to the cranial nerves, 5 cases; acute benign lymphocytic meningitis, 6 cases; localized neuritis following diarrhea or fever or both, 6 cases, and poliomyelitis contacts, 3 cases. Of the 15 cases of poliomyelitis, the stools were positive for virus in 9, in all of which the outcome was fatal. In all other cases the test for virus in the stools was negative.

ECHOLS, New Orleans.

Diseases of the Brain

ELECTROENCEPHALOGRAMS IN POST-TRAUMATIC EPILEPSY. HERBERT JASPER and WILDER PENFIELD, Am. J. Psychiat. **100**:365 (Nov.) 1943.

Jasper and Penfield studied electroencephalographically 81 cases of post-traumatic epilepsy. In 90 per cent a local area in one hemisphere was found in which random spikes or sharp waves were most prominent. In 69 per cent a relatively superficial focus was found in one area without significant abnormality elsewhere. Superficial lesions of the cortex were characterized by

random slow waves and random spikes or sharp waves. This type of activity was found in cases in which seizures occurred shortly after head injury. In 10 per cent of the cases generalized electroencephalographic disturbances were present, and in 3 cases diffuse multiple spikes and sharp waves appeared in the electroencephalogram and were virtually continuous. Bilaterally, synchronous abnormal discharges occurred in 6 cases. In 32 cases surgical extirpation of the seizure focus was carried out. In 94 per cent of this group the preoperative electroencephalogram was a reasonably accurate guide to the border zone of the lesion. In the cases of a single, discrete abnormality of the electroencephalogram surgical excision resulted in notable improvement in 71 per cent of cases, not only so far as incidence and severity of seizures were concerned but in the electroencephalographic pattern.

FORSTER, Philadelphia.

THE EEG IN LATE POST-TRAUMATIC CASES. MILTON GREENBLATT, Am. J. Psychiat. **100**:378 (Nov.) 1943.

Greenblatt studied by means of the electroencephalogram 263 patients who had had head injuries, followed by the appearance of symptoms varying from headache, with or without concomitant symptoms, to convulsions, fainting spells and personality changes. For 32 per cent Greenblatt found normal, for 20 per cent borderline and for 48 per cent abnormal records. Some correlation was present between the severity of symptoms and the degree of electroencephalographic changes; this was noticeable in the study of groups of patients but not in individual cases. No correlation between the interval after injury and the degree of the abnormality could be determined. Patients with post-traumatic seizures had a higher incidence of electroencephalographic abnormality; patients with headache, a lower frequency. It was impossible to correlate either the presence or duration of unconsciousness or the presence of skull fracture with electroencephalographic abnormalities. In the patients with post-traumatic psychoses the incidence of electroencephalographic abnormalities was greater than in the others. In the patients presenting focal electroencephalographic abnormality the focus coincided with the area of injury, skull fracture or deformity, or jacksonian seizures occurred, involving the contralateral extremities.

FORSTER, Philadelphia.

THE WATERHOUSE-FRIDERICHSEN SYNDROME. STUART W. COSGRIFF, Ann. Int. Med. **21**:187 (Aug.) 1944.

Cosgriff reports clinical and laboratory observations on 4 adults with the Waterhouse-Friderichsen syndrome. In the 2 patients for whom serum analyses were made a decrease in sodium and an increase in the nonprotein nitrogen were encountered. These observations are compatible with the results in cases of adrenal insufficiency but bear no relation to the extent of damage observed in the adrenal cortex at autopsy.

The role of hypoadrenalism in the mechanism of this syndrome is not yet established. Therapy should be directed chiefly against sepsis and secondarily toward the correction of possible associated adrenal cortex insufficiency.

GUTTMAN, Philadelphia.

MULTIPLE MENINGIOMA AND MENINGIOMAS ASSOCIATED WITH OTHER BRAIN TUMORS. SILVANO ARIETI, J. Neuropath. & Exper. Neurol. **3**:255 (July) 1944.

Arieti reports a case of multiple meningioma associated with an intracranial aneurysm and 2 other cases in which meningioma was associated with glioma. Microscopic studies and a review of the pertinent literature permit the author to conclude that the embryonal rests of Cohnheim and Ribbert giving rise to the tumors have an inherent neoplastic potentiality which manifests itself at different times in the glial and the meningeal tissues. In case 1 the tumors were all of meningeal origin, but were associated with an aneurysm. Arieti states that if "a developmental defect is considered as a necessary complementary factor in the pathogenesis of this vascular alteration, a local ontogenetic disorder may also be regarded as responsible for all the lesions found in that case."

GUTTMAN, Philadelphia.

A FATAL CASE OF CEREBRAL MALARIA. I. B. SNEDDON, Brit. M. J. **2**:814 (Dec. 25) 1943.

Sneddon reports the case of a man aged 28 who was admitted to the hospital in a semicomatose state, with a history of severe headache, vomiting and fever of three days' duration. There were no abnormal signs referable to the central nervous system. There was moderate leukocytosis; the complexion was muddy, and the pupils were contracted. Examination of the blood showed numerous ring forms of Plasmodium falciparum but no crescents. Twenty-four hours after the intravenous administration of 5 per cent dextrose in isotonic saline solution and the hypodermic injection of quinine dihydrochloride and epinephrine hydrochloride, the patient seemed greatly improved. However, despite continued treatment, he became worse and died on the fourth day after admission. Autopsy established the diagnosis of cerebral malaria. Sneddon presents this case "as a reminder that malaria should be considered in the differential diagnosis of coma and that unless treatment is started early, gross irreversible pathological changes occur in the brain."

ECHOLS, New Orleans.

GUNSHOT WOUNDS OF THE HEAD IN THE ACUTE STAGE. HUGH CAIRNS, Brit. M. J. **1**:33 (Jan. 8) 1944.

Cairns reports the results of a study of 459 men with nonpenetrating head injuries and 506 men with penetrating injuries to the brain. There were 3 deaths among the men with nonpenetrating injuries and 83 among those with penetrating injuries. Of the patients reaching the casualty clearing station in the North African campaign, 20 per cent died of cerebral damage within the next few days. After inadequate operative treatment, it was noted that about 1 of every 4 of the patients who were evacuated had complications of brain abscess or meningitis. However, it has been shown that when patients with head injuries can be segregated at the casualty clearing station, where radical operations are done within twenty-four hours of injury by trained neurosurgeons, the development of intracranial infections can be almost entirely eliminated. With regard to the bacteriology of head wounds, of 36 cases studied, bacteria were present in all but 1, with Staphylococcus aureus predominating. In most cases it was noted that the infection first developed superficially and then spread inward. Although there is still no definite evidence to support the view that sulfonamide compounds are active in the presence of pus, Cairns suggests further trial of these drugs in cases of head wounds in war zones. In a series of 23 men with cerebral wounds seen seventy-two hours after injury, local application of penicillin gave promising results, but further investigation of the technic of its application must be carried out.

ECHOLS, New Orleans.

AN UNUSUAL CASE OF CEREBRAL MALARIA. CHARLES S. D. DON and P. F. MEYER, Brit. M. J. **1**:149 (Jan. 29) 1944.

Don and Meyer report the case of a 22 year old soldier with cerebral malaria in whom 35 per cent of the red blood cells were infected with one or more parasites of Plasmodium falciparum. Thirty-six hours after administration of large doses of quinine dihydrochloride, the patient manifested pronounced cerebral symptoms and appeared to be dying, but responded to supportive measures, consisting of infusions and transfusions. Intensive quinine therapy for the next three days resulted in hyperpyrexia. Recovery was further complicated by hypostatic pneumonia.

ECHOLS, New Orleans.

HEAD INJURIES INVOLVING AIR SINUSES. D. MCKENZIE, Brit. M. J. **1**:652 (May 13) 1944.

McKenzie reports 10 cases of cerebrospinal fluid rhinorrhea due to fractures involving the air sinuses. In 4 cases the condition was the result of fracture by a penetrating missile, received in battle; in the remainder, to blunt injury. McKenzie concludes that indubitable signs that the dura has been torn and that meningitis may be imminent are the presence of cerebrospinal fluid rhinorrhea and intracranial aerocele. Anosmia is suggestive of local injury. Roentgenographic evidence of fracture may be easily overlooked. Preliminary treatment consists in prophylactic administration of sulfadiazine. One should make operative repair of the dura in every head injury with cerebrospinal fluid rhinorrhea rather than risk the dangers of natural repair. McKenzie used both unilateral and bilateral bone flaps. In each case the fistula was located by extradural exploration. There were no complications and no deaths in the author's series.

ECHOLS, New Orleans.

HEREDITARY FAMILIAL TELANGIECTASIS WITH EPISTAXIS AND MIGRAINE. A. M. G. CAMPBELL, Lancet **2**:502 (Oct. 14) 1944.

Campbell reports the case of a young man with telangiectasis whose mother and maternal aunt and grandmother also had the condition. He also had migraine, which preceded the attacks of bleeding from the nasal nevi. The bleeding, in turn, relieved the migrainous attacks. No focal signs pointed to involvement of the central nervous system. The condition had not seriously affected the longevity of the family.

MCCARTER, Boston.

ROLE OF PHYSICAL CONSTITUTION IN THE DEVELOPMENT OF DEMENTIA PARALYTICA. R. ORLANDO and M. ARNDT, Index neurol. y psiquiat. **4**:134 (Feb.) 1944.

Orlando and Arndt studied 214 patients with dementia paralytica from the point of view of Kretchmer's physical types. More than half the patients (52.3 per cent) were asthenic, as were most of the patients with depressive and agitated psychoses. There were more of the pyknic than of the asthenic type among patients with schizophrenic pictures. The asthenic habitus was more frequently associated with tabes in the simple and expansive forms. The number of patients is too small to justify the statement that any particular type is predisposed to the development of dementia paralytica.

SAVITSKY, New York.

Diseases of the Spinal Cord

SUBACUTE NECROTIC MYELOPATHY: A FATAL MYELOPATHY OF UNKNOWN ORIGIN. CHARLES DAVISON and SAMUEL BROCK, J. Neuropath. & Exper. Neurol. **3**:271 (July) 1944.

Davison and Brock report the cases of 3 young persons in whom a myelopathy, with a fairly rapid and fatal course, developed. The characteristic clinical features were progressive paraplegia; sensory impairment, with a level lesion; urinary disturbances, and abnormal findings in the cerebrospinal fluid, not typical of any specific lesion of the cord.

The anatomic features consisted of necrosis or softening of the spinal cord, most conspicuous in the lower dorsal and the lumbosacral region and involving both the gray and the white matter. In 1 case the pathologic process extended from the first cervical to the eighth thoracic segment. A syrinx of the cord and the lower part of the medulla was also present. There was no evidence of an inflammatory reaction. In the first case there was a pronounced mesodermal reaction; in the other 2 cases neither a glia nor a mesodermal reaction was evident.

The etiologic factors were undetermined in these cases, as well as in the other cases reported in the literature. Davison and Brock consider the disease in their cases to be subacute necrotic myelopathy, of unknown origin. They state that the term "myelitis" should be reserved for a condition of purely infectious origin.

GUTTMAN, Philadelphia.

RESULTS OF SURGICAL REMOVAL OF PROTRUDED LUMBAR INTERVERTEBRAL DISCS. BURTON M. SHINNERS and WALLACE B. HAMBY, J. Neurosurg. **1**:117 (March) 1944.

Shinners and Hamby made a follow-up study of patients operated on for herniation of the nucleus pulposus in the lumbar region. A total of 160 operations were performed on 140 patients (20 patients had 2 operations). Protruded disk was encountered in 116 patients, in 111 of whom the lesion was in the lumbar region. The 87 replies received from these 111 patients formed the basis for the figures compiled. Of this number, 49.5 per cent said they were cured, 48.3 per cent thought they were improved, and 2.3 per cent stated that in some ways they were worse than before operation. Fifty-four per cent had residual pain in the back, the leg or both; 87.4 per cent were working, only 4 having changed occupation; 20.3 per cent of the compensation group (28.4 per cent) still receive compensation; 57.3 per cent had pain in the leg or back on working; 92 per cent were glad they had the operation, and 4.8 per cent said they were sorry.

A striking parallelism in the results of operation was noted between patients receiving compensation and private patients.

WHITELEY, Philadelphia.

EPIDEMIC OF POLIOMYELITIS IN ZURICH IN 1937. W. ABEGG, Arch. f. Kinderh. **125**:166 (April 24) 1942.

Abegg reports observations on 167 patients with poliomyelitis in the course of the epidemic in Zurich, Switzerland, in 1937. The treatment consisted chiefly in the administration of serum and blood transfusions. The serum was a mixture of convalescent and so-called contact serum. The efficacy was not entirely convincing. Of the 167 patients, 62.3 per cent recovered; 19.2 per cent improved; 8.9 per cent did not improve, and 9.58 per cent died. Of the 16 patients who died, 7 were

moribund at the time of hospitalization. Follow-up observation revealed that in 10.8 per cent of the patients the paralysis was so severe that they will be severely handicapped for life. No defects aside from the paralysis remained. The severe meningitic symptoms produced neither impairment of intelligence nor signs of parkinsonism. The changes in character suggested by the parents of some of the children were the result of relaxation in discipline, due to pity rather than to organic changes.

J. A. M. A.

Peripheral and Cranial Nerves

CRANIAL-NERVE PALSIES WITH HERPES FOLLOWING GENERAL ANAESTHESIA. J. H. HUMPHREY and MARGARET MCCLELLAND, Brit. M. J. **1**:315 (March 4) 1944.

Humphrey and McClelland report 13 cases of cranial nerve palsy following anesthesia, in 2 of which the outcome was fatal. The use of no one anesthetic was common to all cases. The severity of the condition varied from subjective trigeminal anesthesia to encephalitis. Twenty-four to forty-eight hours after administration of a general anesthetic the patients complained of a sense of coldness, numbness or tightness around the lips, which spread along the whole distribution of the fifth nerve on both sides. Difficulty in swallowing was also experienced. Circumoral herpes of the febrile type appeared on about the third postoperative day. The fifth and seventh nerves were most frequently involved, but the third, fourth, sixth, tenth and twelfth cranial nerves were affected in some cases. When improvement occurred, it began from the fifth to the tenth day; rapid recovery followed in cases of milder disturbance, whereas with the more severe form residual subjective changes were still apparent five months later. Clinical evidence and the results of experimental investigation strongly favor a toxic theory. The authors suspect that trichloroethylene, which had been used in the anesthetic machine, had combined with the soda lime, with the production of dichloroacetylene, and they conclude that, until further investigations have been made, trichloroethylene should not be used where there is any possibility of its coming in contact with soda lime.

ECHOLS, New Orleans.

EARLY DIAGNOSIS OF PERIPHERAL NERVE INJURIES IN BATTLE CASUALTIES. W. R. RUSSELL and A. B. HARRINGTON, Brit. M. J. **2**:4 (July 1) 1944.

Russell and Harrington describe in detail neurologic methods for examination of wounded extremities for nerve injury. These procedures can be used by surgeons in forward battle areas. Illustrations of the methods are included. A simple technic of recording nerve function is explained. The dangers of excessive splinting of the fingers in the early treatment of nerve injuries are emphasized. Maintenance of range of movement of the joints is all that is necessary in the early treatment of injuries to the nerves of the lower extremity. The importance of attention to the patient's morale is stressed.

ECHOLS, New Orleans.

SUPERIOR SULCUS TUMOR (PANCOAST). B. A. DORMER, F. J. WILES and J. FRIEDLANDER, Lancet **2**:312 (Sept. 2) 1944.

Dormer, Wiles and Friedlander describe a case of a tumor of the superior pulmonary sulcus associated with pain in the shoulder and arm, Horner's syndrome and signs of pressure on the ulnar nerve. There was roentgenographic evidence of infiltration of the apex of the lung, but not of involvement of bone. As a result of complete paralysis of the right recurrent laryngeal nerve, there was inability to shout or sing. The condition was inoperable. A specimen was taken for biopsy, but it was impossible to be certain of the origin of the tumor. The general structure was not unlike that sometimes seen in carcinoma of the bronchus.

Pancoast stated the belief that the type of tumor to which his name has been attached comes from a remnant of the branchial cleft. His syndrome may be due to this or to any other tumor of the superior pulmonary sulcus. All authors are agreed that, in view of their location, such neoplasms are always fatal.

MCCARTER, Boston.

NEUROLOGICAL COMPLICATIONS OF SERUM AND VACCINE THERAPY. R. R. HUGHES, Lancet **2**:464 (Oct. 7) 1944.

Hughes reports 6 cases of neurologic complications following serum or vaccine therapy. Other authors have pointed out that of all serums, vaccines and antitoxins, tetanus antitoxin most commonly causes complications of this nature. Allen classified such complications into four types: radicular, neuritic, polyneuritic and central. In the radicular type which occurs in half the cases, an attack of serum sickness occurs five to ten days after injection of serum, and pain, weakness and wasting develop in the shoulders. Sensory changes are slight or absent. The neuritic type is confined to a peripheral nerve, with onset of paralysis twenty-four to forty-eight hours after the appearance of serum sickness. The polyneuritic type is characterized by generalized peripheral neuritis. The central type shows "evidence of cerebral involvement, usually papilledema accompanied in some cases by a meningeal reaction or focal cerebral lesion." The cranial nerves have also been reported to be involved.

Hughes points out how closely these complications resemble the disturbances said to be due to virus infection. "Further investigation of the etiology of these conditions is urgently required."

MCCARTER, Boston.

Treatment, Neurosurgery

BORDERLINE CASES TREATED BY ELECTRIC SHOCK. ABRAHAM MYERSON, Am. J. Psychiat. **100**:355 (Nov.) 1943.

Myerson reports the results of electric shock therapy in 10 cases in which either the patient was noncommittable or the condition was not amenable to clearcut diagnosis. These cases included instances of fixed depressive ideas, depressive states relating to real life situations, obsessive-compulsive states, anhedonic unreality and, in 1 case, anorexia nervosa, which shifted to bulimia. Treatments were administered in the outpatient department, with temporary improvement in each case.

FORSTER, Philadelphia.

RESULTS OF HOSPITAL TREATMENT OF ALCOHOLISM. JAMES H. WALL and EDWARD B. ALLEN, Am. J. Psychiat. **100**:474 (March) 1944.

Wall and Allen report the results of hospital treatment of 100 men admitted because of alcoholism. Eighty-one of the series had no psychosis. There was a high incidence of alcoholism among the relatives of

the patients. In 59 cases the mothers of the patients had been oversolicitous and the fathers had been successful and forceful. Study of the sexual life and the social and interpersonal relationships of the patients revealed precarious adjustments. Drinking had usually begun at an early age and had been continued for long periods, the average being fifteen years. The authors recommend a period of treatment of six months to a year. The therapeutic regimen consists in attention to physical defects, physical therapy and psychotherapy, the last being directed toward appreciation of the gravity of the situation and the underlying psychologic features, the need for total abstinence and the evaluation of the patient's assets. Follow-up studies revealed that 33 per cent did not improve, 19 per cent were drinking, but their condition had improved and 24 per cent were recovered.

FORSTER, Philadelphia.

PERIPHERAL NERVE SURGERY: TECHNICAL CONSIDERATIONS. R. GLEN SPURLING, J. Neurosurg. **1**:133 (March) 1944.

In this article the technic and routine followed in treatment of peripheral nerve injuries at the Walter Reed General Hospital are described. Among the general principles advocated is the postponement in closure of battle wounds until they are reasonably clean. Two weeks after this secondary suture exploration for nerve repair is performed. At this time chemotherapy, hemostasis, mobilization and correct positioning of joints, freedom from nerve tension and nerve transplantation are important items of treatment. At operation electrical stimulation of exposed nerve trunks is valuable in diagnosis of anatomic severance.

This hospital follows the radical exposure of peripheral nerve injuries in all cases except those in which the symptoms show rapid improvement. If impulses still traverse the scar, only neurolysis is effected; end to end suture is performed in cases of complete severance. Use of fine tantalum sutures and cuffs of tantalum foil has facilitated successful nerve anastomosis.

WHITELEY, Philadelphia.

TREATMENT OF THE PAINFUL PHANTOM LIMB BY REMOVAL OF POST-CENTRAL CORTEX. C. G. DE GUTIÉRREZ-MAHONEY, J. Neurosurg. **1**:156 (March) 1944.

De Gutiérrez-Mahoney believes that pain is felt in every case of phantom limb, which, in turn, nearly always follows amputation, but that it is seldom disabling. The exact cause of the condition has not yet been determined, but it is probably due to stimulation of peripheral nerves, with the pulses reaching consciousness.

The simplest and most effective way of dissolving this phantom is to interrupt the centripetal pathway by removing the corresponding portion of the postcentral cerebral cortex. The author reports a case in which operation was performed more than two years before, with no recurrence of symptoms.

WHITELEY, Philadelphia.

TREATMENT OF MENINGOCOCCAL MENINGITIS WITH PENICILLIN. MANSON MEADS, H. WILLIAM HARRIS, BERNADO A. SAMPER and MAXWELL FINLAND, New England J. Med. **231**:509 (Oct. 12) 1944.

Meads, Harris, Samper and Finland report observations on 9 unselected patients with meningococcic meningitis admitted to the Boston City Hospital during April 1944. The ages of the patients ranged from 14 to 58 years. Seven patients were acutely ill and irrational. One was acutely ill and rational, and 1 was only moderately ill when first seen. The duration of the acute illness before hospitalization varied from one to seven days, with an average of about three days. The usual laboratory studies, including examination of the cerebrospinal fluid, were performed. Five of the patients had concomitant meningococcemia. All the patients were given the calcium salt of penicillin intrathecally and intramuscularly.

The clinical response to penicillin is slower than that to the sulfonamide compounds, for the following reasons: Biochemical and bacteriologic abnormalities in the spinal fluid persist longer; there may be recurrences; the meningococcus carrier state may persist; the treatment is difficult, and, finally, one may eventually have to resort to the sulfonamide compounds. Also, strains of the type I meningococcus vary greatly in their susceptibility to penicillin. Those studied in this series of patients resembled the relatively resistant strains of Staphylococcus aureus and Streptococcus viridans.

The authors conclude from their observations that the sulfonamide compounds are the drugs of choice in the treatment of meningitis due to the type I meningococcus and that penicillin may be effective in treatment of this form of meningitis in the doses used (from 190,000 to 1,155,000 Oxford units). However, the response is less favorable than that following the use of sulfonamide compounds.

GUTTMAN, Philadelphia.

THE TREATMENT OF SCIATICA: AN ESSAY IN DEBUNKING. ARTHUR HURST, Brit. M. J. **2**:773 (Dec. 18) 1943.

Numerous and divergent views regarding the pathogenesis of sciatica have been expressed, and the methods of treatment have been as varied. A review of the therapy of sciatica from 1901 to 1943 corroborates this statement. Methods which have been tried include injection of various drugs into the nerve, the intervertebral space and the myalgic spots; manipulation; application of plaster cast; removal of herniated intervertebral disk or lateral intervertebral joint, and the application of "fuming hydrochloric acid." As a rational method of treating sciatica, Hurst recommends complete rest in bed from the onset of symptoms, with immobilization in a plaster spica only in cases of severe pain. With this procedure, he insists on simple psychotherapy, which promotes the expectation of rapid and complete recovery. A few patients, who fail to respond after one month of such conservative treatment, will probably require relief of root pressure by removal of a herniated intervertebral disk.

ECHOLS, New Orleans.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

GEORGE D. GAMMON, M.D., *Presiding*

Regular Meeting, April 28, 1944

Spontaneous Subarachnoid Hemorrhage with Coarctation of the Aorta: Report of a Case with Recovery. DR. RICHARD HEARNE.

Coarctation of the aorta is a rare condition. This fact, together with the neurologic changes in the present case, suggests that a report would be of interest.

REPORT OF CASE

H. A., a Negro aged 21, unmarried, entered the Philadelphia General Hospital on Jan. 3, 1944. He had been rejected for Army service in the fall of 1943 because of "heart trouble," but his mother declared that he had always been healthy until the day before admission to the hospital. At that time he suddenly had a severe bursting headache, followed by fever, sweats and cramps in his neck, back and legs.

Examination on admission was incomplete because the patient was irrational, hyperactive and uncooperative. The neck was rigid; the deep reflexes were hyperactive throughout; the Brudzinski and Kernig signs were present, and the patient was incontinent of urine and feces. The spinal fluid contained bright red blood, the last of the specimen being as bloody as the first. The blood pressure in the right arm was 220 systolic and 125 diastolic. Except for leukocytosis, with a count of 18,200, the results of laboratory studies were without significance.

Three days after admission to the hospital the patient was transferred to the neurologic service of Dr. A. S. Tornay. Examination revealed that the patient was strong and well developed. He was lying in a position of opisthotonos, was stuporous and did not respond to efforts made to arouse him. The neck was rigid, and the head was turned sharply to the left and fixed in that position. The deep reflexes were somewhat increased in the right arm and leg, and there was increased resistance to passive motion in these limbs. The abdominal and cremasteric reflexes were absent. The spinal fluid was still uniformly bloody.

Examination of the chest showed enlargement of the heart, and there was a diffuse, heaving apical impulse. A high-pitched systolic murmur could be heard over the entire precordium. However, the most characteristic feature of this murmur was a pronounced, bilateral parasternal accentuation, which even extended down into the epigastrium. A diastolic murmur was also heard over the aortic area and in the left third interspace. Deep subcutaneous vessels, approximating in size that of a normal radial artery, could be felt pulsating over the chest. These vessels were especially numerous in the infrascapular and subscapular regions. The pulse over the femoral arteries was small and weak, with a definite lag when it was compared with the radial pulse. Neither the pulse in the popliteal artery nor that in the dorsalis pedis artery could be felt on either side. The blood pressure was 205 systolic and 80 diastolic in the right arm and 150 systolic and 75 diastolic in the left arm. No blood pressure could be obtained in the legs.

Roentgenograms of the chest showed a moderately enlarged heart with a configuration characteristic of hypertension. There were prominence of the ascending aorta and absence of the aortic knob of the descending aorta. However, the lower margins of the ribs were only slightly eroded. An electrocardiogram showed beginning left axis deviation.

The patient's neurologic signs and his headache gradually subsided after a stormy course of a few days, during which he was kept under heavy sedation. He was discharged home, apparently completely recovered, three and a half weeks after admission.

Comment.—This patient presented a classic picture of coarctation of the aorta with one of its commoner complications. The principal points in establishing the clinical diagnosis were: (1) hypertension in the arms, (2) absence of detectable pulse or blood pressure in the legs, and (3) demonstration of the collateral circulation circumventing the obstructed aorta.

DISCUSSION

DR. ANTHONY S. TORNAY: This patient was admitted to the Philadelphia General Hospital with the classic signs and symptoms of meningeal irritation. He was sent to the fever ward, and his condition, at the time of admission, was suspected to be meningococcic meningitis. A spinal tap revealed bloody spinal fluid. Several days later the patient was reassigned to service 2 of the neurologic ward.

At this time I felt the patient's condition was malignant hypertension, with one of its complications, spontaneous subarachnoid hemorrhage. The course was very stormy; and when he began to improve, I was surprised to have the resident, Dr. Hearne, ask me whether I could detect any pulsations of blood vessels of the lower extremities on palpation. I failed to feel the pulsations of the tibial or the popliteal vessel. Also, it was impossible to obtain blood pressure readings in either lower extremity. On close examination there was also noted some dilatation of the superficial blood vessels over the chest. This, with the roentgenographic confirmation of the clinical diagnosis of coarctation of the aorta, led my colleagues and me to believe we had an unusual problem in this patient.

The following points should be emphasized in connection with this condition. First, in about 13 per cent of all cases of coarctation of the aorta a vascular complication exists. A vascular anomaly in one part of the body sometimes means that other vascular abnormalities are present. Furthermore, the elevation of the blood pressure above the thorax leads to intracerebral complications.

The patient improved, walked out of the hospital and is walking about the streets of Philadelphia, with the "sword of Damocles" hanging over his head.

DR. HELENA RIGGS: My associates and I have studied the incidence of miliary aneurysm in about 2,000 consecutive autopsies and, oddly, we have found no coincidence with congenital defects of the heart. In all the 45 cases in which ruptured aneurysm was present there was an associated chronic degenerative cardiovascular disease, but not of the congenital type.

DR. GEORGE D. GAMMON: Dr. Hearne has done a service in calling attention to another cause of spontaneous subarachnoid hemorrhage. Few of the textbook discussions of the cause of this condition include coarctation of the aorta. I believe Brain mentioned it in his book. I looked up the matter at one time, when I was studying the case of a patient at Children's Hospital, in the service of Dr. James Reilly.

A boy aged 11 years had a sudden onset of headache followed by stupor and was admitted to the hospital with a diagnosis of meningitis. The blood pressure in both arms was 160 systolic and 110 diastolic. The neck was stiff, and he was semistuporous. Spinal puncture revealed fresh blood, without xanthochromia.

Over the heart was noted a loud, blowing systolic murmur, best heard to the left of the sternum in the third inner space. After spinal puncture the boy showed improvement for five days, during which time renal studies were carried out in order to determine the mechanism of the hypertension.

Urinalysis gave entirely normal results except for specific gravity of 1.016 and, on one occasion, 1.007, with fluctuation between these levels. A urogram of the kidney revealed nothing abnormal except for slight ptosis. These negative results led to reexamination of the patient in an effort to determine the cause of the hypertension.

The resident, Dr. E. P. Morris, noted that the blood pressure was unobtainable in the lower extremities. The intercostal arteries were pulsating, and two large arteries passed downward on the lateral thoracic wall from the axilla for a distance of about 6 inches (15 cm.).

Roentgenographic study showed no evidence of erosion of the ribs. The heart was slightly enlarged on the right side but otherwise appeared normal in the roentgenogram. A clinical diagnosis of coarctation of the aorta was made.

The boy continued to improve for a week and then suddenly became stuporous and cyanotic, and the blood pressure rose to 250 systolic and 170 diastolic. He was bled from the brachial artery; but the blood pressure fell only to 190 systolic and 170 diastolic, and he died of respiratory failure.

Lumbar puncture revealed fresh blood, and it was believed that he had had another hemorrhage.

Autopsy was confined to the chest. The right side of the heart was enlarged. The left ventricle showed extreme hypertrophy. At the site of the ductus arteriosus the aorta narrowed abruptly to about 0.8 cm. in external diameter. Beyond this point it ballooned out to form an unusually prominent thoracic segment, which narrowed down to normal size only at about the level of the diaphragm.

The intercostal arteries were all prominent, particularly the first and second. At the constriction, the aorta permitted the passage of a 2 mm. probe. The lumen of the ductus arteriosus was obliterated.

The kidneys showed little change, but an occasional glomerulus had undergone thickening of the capsule and partial hyalinization. In other words, the condition was not renal hypertension. The larger blood vessels of the kidney were not abnormal.

Unfortunately, I could not examine the brain, and I do not know the condition of the vessels there; but from the clinical picture there seems little doubt that the boy died of subarachnoid hemorrhage. He had a history of minor headaches, but nothing of any significance before this sudden onset of hemorrhage.

I should like to ask Dr. Hearne how many cases of spontaneous subarachnoid hemorrhage with coarctation of the aorta have been reported in the literature. In what percentage of cases is subarachnoid hemorrhage due to coarctation of the aorta?

DR. RICHARD HEARNE: In 1928 Hamilton and Abbott reported a total of 211 cases of coarctation of the aorta verified at autopsy (*Am. Heart J.* **3**:381, 1928), and in 20 of this number death was due to cerebral hemorrhage. In 18 of these cases the hemorrhage was subarachnoid. Since 1928, 2 cases of subarachnoid hemorrhage have been reported in the literature. The number of cases similar to the one reported here is probably small.

Meningitis Due to Infection with Torula Histolytica: Report of a Case. DR. JOSEPH E. SNYDER.

The first report of a case which can be almost surely identified as one of torulosis of the central nervous system was made by Zenker in 1861. At the present time less than 100 cases have been recorded. The organism responsible for this unique disease was carefully studied by Stoddard and Cutler in 1916. They named it Torula histolytica, which Freeman and Wiedman considered a misnomer because their studies indicated that it does not have lytic properties for nerve tissue.

T. histolytica is a pseudoyeast which involves many internal organs, particularly the brain and the spinal cord, presenting three types of lesions. These lesions may be, first, diffuse granulomatous meningitis; second, small granulomas or cysts in the cortex, and, third, deeply placed lesions, sometimes solid but more often cystic. The disease apparently does not occur frequently enough, or is not diagnosed often enough for it to be considered in the differential diagnosis as often as it should be. Torular infection should be considered in cases of atypical meningeal irritation in which the usual pyogens are not encountered. India ink preparations of the spinal fluid provide a ready means of identification of the organism and differentiate between the torulas and red blood cells, for which the organisms are often mistaken.

The following case is reported because it is, to my knowledge, the first case in which penicillin was employed and because its pathologic lesions, particularly those of the central nervous system, were studied.

E. M., an 8 year old white girl, was well until two and a half years before her admission to the University Hospital, when there developed an acute staphylococcic osteomyelitis of the femur and humerus which was refractory to sulfathiazole and became chronic, with sequestration and the formation of multiple draining sinuses. On admission to the hospital for penicillin therapy of the osteomyelitis, she had multiple draining sinuses, mild weakness of the right sixth nerve and definite nuchal rigidity and complained of frontal headache, which she had noted for the preceding two weeks. The vital signs were normal except for a slight elevation of blood pressure. The blood and urine showed no abnormalities. Twenty-four hours later she suddenly became comatose, at which time the head and eyes turned to the left with lateral nystagmus, and she went into opisthotonos with generalized rigidity except for paralysis of the right side of the face. Thirty minutes later she regained consciousness and seemed fairly alert. Three lumbar punctures at five day intervals showed the spinal fluid to be under increased pressure. The fluid obtained on the first tap was slightly blood tinged, but the succeeding two specimens were clear. Microscopic examination revealed between 60 and 100 cells per cubic millimeter in each of the specimens of fluid, which were reported as red blood cells but were probably torulas. Cultures of the first two specimens showed an organism which was reported as "Monilia" and was regarded as a contaminant. The third specimen re-

vealed the same organism, which, when examined in india ink preparations, was shown to be T. histolytica. The penicillin, which had already been given in the amounts of 90,000 Oxford units daily, was increased to 120,000 units, supplemented by intrathecal administration of 10,000 units daily. In addition, large doses of sodium iodide and sodium sulfadiazine were given intravenously. The patient appeared to improve for a short time; then, although she had received a total of nearly 3,000,000 units of penicillin, she began to have numerous convulsive seizures and died of sudden spontaneous bilateral pneumothorax.

At autopsy, the most striking lesions were found in the brain. The meninges were smooth and glistening, but the subarachnoid and ventricular fluid was pearly gray and cloudy. The brain was fixed in solution of formaldehyde U. S. P., in 1:10 dilution, for one week. Transverse sections of the brain revealed many small single multilocular cysts, occurring chiefly in the gray matter of the frontal and parietal lobes. These cysts were sparsely scattered over the ependymal surfaces of the cerebellum. The entire basal ganglion system was replaced by a mass of multilocular cysts containing a pearly gray, gelatinous material. Microscopic examination revealed the cysts to be extremely thin walled, with no surrounding inflammatory reaction. The adjoining cells appeared to be somewhat compressed. The cysts contained large numbers of the torulas. The torulas were also seen in the meninges, but there was no inflammatory reaction. The lungs showed small blebs over the pleural surfaces, extending down into the parenchyma. The liver, spleen and lymph nodes were greatly enlarged. Histologic studies showed small cyst formations containing torulas in all organs except the heart muscle, including the vertebral marrow and the retina. The normal architecture of the lymph nodes was completely destroyed and replaced by variously sized, thin-walled cysts containing torulas. It is of interest to note that numerous antemortem and a postmortem blood culture failed to show the organism.

In this case the portal of entry of the organism could not be determined. The diagnosis was delayed by failure to recognize the torulas in the spinal fluid, the organisms being mistaken for red blood cells. Previous case reports indicate that in many instances these organisms have been similarly mistaken for red blood cells or for lymphocytes. Penicillin in the dosage employed failed to alter the course of the disease, though the osteomyelitic process promptly subsided.

DISCUSSION

DR. HELENA RIGGS: Dr. Snyder is to be congratulated that the diagnosis was made before death. I have had 2 cases of blastomycotic involvement of the central nervous system, in both of which the diagnosis was made post mortem. The clinical aspects of these cases were so dissimilar that it might be well to outline the symptoms.

The first case was that of a physician aged 50 who, during a period of a year and a half, showed pronounced mental deterioration. He was brought into the Philadelphia General Hospital with a presumed diagnosis of dementia paralytica, which was not confirmed serologically. While in the hospital, he showed such emaciation that a diagnosis of amyotrophic lateral sclerosis was considered. He died with the diagnosis unestablished. There had been no signs referable to meningeal irritation.

At autopsy the meninges showed extreme thickening and a "boiled egg white" appearance, and the brain was shrunken. Histologic examination revealed chronic meningitis of both the brain and the spinal cord, with torulas around the choroid plexus and over the base of the brain. The diagnosis was confirmed by Dr. F. Weidman.

The second case was that of a Negro youth aged 17. He was admitted to the hospital with a history of severe headache, stiff neck and coma and died six hours after admission, eighteen hours after onset of the first symptoms. The spinal fluid contained 800 polymorphonuclear leukocytes per cubic millimeter, with a sterile culture. The condition in this case was not torulosis, but sporotrichosis.

At autopsy there were bruiselike areas over one surface of the brain, and histologic examination showed a myriad of yeastlike, or fungus-like, organisms filling these areas and the subarachnoid space, with a secondary reaction of lymphocytes.

In the first case the condition of the nervous system was extremely chronic, without signs of meningeal irritation; in the second case there was a picture of acute purulent meningitis.

DR. MATTHEW MOORE: The case reported by Dr. Snyder is truly an extraordinary one in view of the wide dissemination of the so-called torulas, involving practically every organ of the body. At this point, may I indicate that the organism is not a torula; neither is it histolytic, but, as Dr. Snyder intimated, properly belongs to the cryptococci—Cryptococcus hominis, or Cryptococcus meningitidis.

It is important to emphasize what Dr. Riggs has stated with regard to the symptoms in cases of torulosis. A review of the reported cases indicates that almost invariably, with the exception of a few cases in which the diagnosis was made ante mortem, the clinical diagnoses have been chiefly brain abscess, brain tumor or tuberculous meningitis. Tuberculous meningitis seems to have been the most frequent diagnosis, because of the rather chronic course of the disease.

Dr. Greenfield and I presented before this society a case of cryptococcic meningoencephalitis in which the meninges and brain were notably involved (Meningoencephalitis Due to Cryptococcus Hominis, ARCH. NEUROL. & PSYCHIAT. **40**:1054 [Nov.] 1938). More recently, we have examined the brain of a man aged 68 who had been in the Graduate Hospital of the University of Pennsylvania during the early part of 1943. He had complained of intense headache for about eight days before his admission. The clinical diagnosis was either abscess of the brain or glioma. Ventriculographic studies were carried out, and subsequently operation was performed for a tumor of the temporal lobe. No tumor was exposed. He died eight days after operation. Tissue studies of the brain revealed intense meningoencephalitis, due to cryptococcic meningitis. It may be pointed out that in cryptococcic invasion the meninges are not involved alone, but there is an accompanying involvement of the brain itself. There is no inflammatory reaction on the part of the brain tissue. It merely is pushed aside and compressed by the growth of the cryptococci and does not undergo histolytic change, nor is there inflammation or glial reaction of any note at the periphery of the cerebral lesions.

Did Dr. Snyder note foreign body giant cells in his case? In some cases huge, multinucleated giant cells have appeared in or about the cerebral lesions, a feature reported in our first case.

I wish that Dr. Snyder would express an opinion regarding the possible relation of the widely scattered

lesions to the use of penicillin, in that this drug, instead of aborting the disease, may have acted symbiotically and thereby have contributed to the dissemination of the lesions throughout the body.

DR. JOSEPH E. SNYDER: In the examination I saw a cell that could be considered a giant cell. Such cells were certainly rare.

With regard to the effect of penicillin I am uncertain. If penicillin did no more, it retarded the progress of the "osteomyelitis," and if the organism entered the body through the draining sinuses and was present in these sinuses, their healing should have some effect on the organism, but certainly not a curative one.

DR. D. SCOTT: In view of the careful way in which the clinical material has been assembled in this case, it is interesting to restudy the electroencephalogram, with particular attention to the pertinent information which it brought to light.

At the time this patient was studied, he had been recently admitted to the hospital, and the diagnosis was uncertain. However, some examiners expressed the opinion that possibly the disorder was focal epilepsy.

From the electroencephalogram which shows simultaneous tracings from the left and the right temporal area, one can see that there is complete symmetry of the pattern, which is characterized by the appearance of persistent, slow, irregular waves. This type of activity was obtained from all areas of the cortex, although it was slightly more prominent in the left frontal area than elsewhere. This was reported as indicating the existence of a diffuse, degenerative process, and it was stressed that there was no evidence in favor of a single irritative focus. It is now known that such a diffuse process was present, which was both degenerative and pressure producing, thus giving optimum conditions for the type of cortical irritation that usually results in prominent electrical activity.

While the electroencephalogram, of course, is only one of several means which helped in arrival at the diagnosis, I believe it was a valuable contribution in this instance because of the possibility of obtaining a clearcut differentiation between a focal and a diffuse lesion.

DR. GEORGE D. GAMMON: Can Dr. Snyder state where these organisms live outside the human body?

DR. JOSEPH E. SNYDER: So far as I am aware, no one knows where these organisms live. There are other species that are fairly omnipresent, but this particular organism has not been seen except in cases of cryptococcic meningitis.

Reeducation of the Aphasic Patient. DR. FRANK P. BAKES.

The speech examination of an aphasic patient is primarily a matter of psychologic testing, with a view to determining what intellectual functions are intact. My colleagues and I try to determine what sensory avenues are available for training and what motor abilities remain for expression. We test particularly for auditory and visual function, on the sensory side, and for ability to write and speak, on the motor side. We also determine whether he can understand what he writes and whether he can write from dictation, either in print or in script.

Most aphasic patients are under considerable emotional tension and are beset with worries. Our approach then leads us to sympathetic handling and understanding. We must also provide reassurance and encouragement because these persons are easily discouraged, as a result of their slow progress.

I should like to describe briefly two methods which have not yet been employed extensively but which seem to give promise of effective use. The first is known as the motokinesthetic method, originated by Sara M. Stinchfield and Edna Hill Young (Children with Delayed or Defective Speech, Stanford University, Calif., Stanford University Press, 1938). This method was devised especially for the speech training of children with delayed speech, but it has been found useful for other types of speech disorders. The method consists primarily of actually manipulating the articulatory organs in such a way as to help the subject gain a kinesthetic impression of the proper position of the lips, tongue, jaw, etc., in producing the various speech sounds. For example, to quote from Stinchfield and Young, "to produce the 'p' sound, let the trainer place his thumb and forefinger below the lower lip, moving it upward until the two lips meet in closed position, not allowing them to become taut in that position or to press upon each other with any degree of tension. Immediately upon the closure, the trainer, without lifting her hand from contact with the jaw, brings the lower lip and jaw downward, usually securing the 'puff' in question as the lower lip parts from the other."

Another method, reported by Grace Fernald (Remedial Techniques in Basic School Subjects, New York, McGraw-Hill Book Company, Inc., 1943), is known as the kinesthetic method and is used primarily as a remedial technic in teaching the basic school subjects. The method could well be called a "tactual kinesthetic" technic, as a great deal of emphasis is placed on the importance of finger contact with the paper on which a word is written or printed. In this procedure, the teacher writes in large script in crayon on a strip of paper the word which the child is to learn. The child then traces the word with his index finger, sounding it as he progresses through the word. After a few repetitions, he writes the word without copying it. This is especially effective in cases of disturbances in spelling and reading. Dr. Fernald suggests that she and her associates ignore the matter of handedness and seem to secure good results without emphasis on training the dominant hand.

DISCUSSION

DR. HENRY WYCIS: Has Dr. Bakes tried the use of music in the reeducation of aphasic patients? This might be of special interest in view of the fact that some aphasics can sing words and tunes whereas they are unable to speak them.

DR. MATTHEW MOORE: What hope of success can Dr. Bakes offer a patient who has had aphasia for two or three years?

DR. FRANK P. BAKES: I cannot say, for we have not used the method long enough to determine that. In the cases I reported, I think that the training was begun shortly after onset of the aphasic condition.

We hope to employ these methods with some of the patients we are getting. We did start with 1 patient last summer; unfortunately, after only a few weeks, he was unable to continue, and we were unable to evaluate the results.

CHICAGO NEUROLOGICAL SOCIETY

R. P. MACKAY, M.D., *President, in the Chair*

Regular Meeting, May 9, 1944

A Complication of Prefrontal Lobotomy. DR. LLOYD H. ZIEGLER† and DR. CARROLL W. OSGOOD, Wauwatosa, Wis.

The cases of 7 of 16 surviving patients were reported in which edema or bullae (or both) of the lower extremities appeared soon after prefrontal lobotomy. Theoretic possibilities, such as injury to the cortical center for the leg and foot and the paracentral lobule and the branches of the anterior cerebral artery were discussed.

The authors stated that basic research is needed to explain this complication, which is usually mild and passes away in a month or two. They expressed the opinion that a larger opening in the skull should be made to deal better with anomalies of the brain and skull that might be encountered.

DISCUSSION

DR. PERCIVAL BAILEY: The first roentgenogram seemed to indicate that the incision was too far back. It seemed to be 1.5 cm. back of the coronal suture. It must have entered the hypothalamus. That may explain in part the symptoms referable to the rectum and bladder. The illustration does not represent the usual course of the anterior cerebral artery. The artery usually has a large branch which leaves the corpus callosum for the callosomarginal sulcus, leaving only a small minor branch passing over the corpus callosum.

DR. CARROLL W. OSGOOD, Wauwatosa, Wis.: We were interested in the fact that no one else had reported this complication, and we wondered why that was. It may be that surgeons did not have the patients under as close observation as we had in the sanatorium. We thought it worth while to call attention to this edema, as other reports may be made to bear out our observation. Two patients had considerable edema of the legs prior to operation and did not have it afterward. One was a very agitated woman, who stood practically all the time. The edema in her case may have been hypostatic. Since the operation, she is more active, and the edema has disappeared.

DR. PAUL C. BUCY: It is probably erroneous to say that this edema has to do with the paracentral lobule. If this area of the brain were involved, it is likely that there would be paralysis and a Babinski sign. I think the edema results from injury to the anterior part of the precentral area, that which Fulton called the premotor area, which has to do with vasomotor phenomena.

Lesions of the Cauda Equina Caused by Rupture of Intervertebral Disk. DR. ADRIEN VERBRUGGHEN.

Effects of Implantation of Methylcholanthrene in the Brain of a Dog. DR. PERCIVAL BAILEY, DR. KENTARO SHIMIZU and DR. EDWARD W. DAVIS.

This paper has been published elsewhere (*J. Neuropath. & Exper. Neurol.* **3**:184-188 [April] 1944).

Treatment of the Convulsive State at the Illinois Security Hospital. DR. A. J. ARIEFF.

This is a preliminary report on the therapy of the convulsive state in a series of 21 patients at the Illinois Security Hospital.

The convulsive state was associated with a psychosis in 8 patients, 4 of whom had paranoid states with deterioration and 4 schizophrenia; 2 patients were mentally defective; 6 patients had organic disease of the brain (in 1, due to trauma; in 1, to encephalitis; in 1, to meningovascular syphilis, and in 3, to chronic alcoholism); 4 had conditions classified as confusional states, and 1 had a constitutional psychopathic state. Deterioration was evident clinically in 11 of these patients, or approximately 50 per cent. Ideas of persecution were common in the whole group because of confusion and lack of insight.

All the 21 patients had major seizures. Fifteen patients also had minor and equivalent states. The ages ranged from 24 to 73 years, with a median of 41. The average stay in the institution was nine years, with a range of from one to thirty-two years. The frequency of seizures varied from two to one hundred a month.

Patients were observed only over a period of six months. Six patients had a remission of all seizures for from three to six months. All but 1 of these patients showed coincidental improvement in behavior. Twelve patients showed improvement in that 4 had remissions of two months and the seizures of all decreased in number up to 90 per cent of the number occurring previously. The symptoms of the actual psychosis remained unchanged.

In 1 patient therapy seemed to have little effect. Practically all the patients presented behavior problems. The behavior of 2 patients was considered good, and that of 17 of the 21 patients was improved. The behavior was unchanged in 2 patients. This evaluation of the behavior was determined by interviewing the attendants in the wards. A decrease in the confusional incidents was likely to result in more cooperative behavior.

Five patients were treated with phenobarbital alone. Three were treated with diphenylhydantoin sodium and phenobarbital; 8, with sodium bromide and phenobarbital; 3 with diphenylhydantoin sodium and sodium bromide, and 2 with the combination of bromide, phenobarbital and diphenylhydantoin sodium. One received a proprietary tablet containing belladonna alkaloids in addition to phenobarbital. With 3 patients treatment with diphenylhydantoin sodium was discontinued after it was found ineffective. This drug did not have any superior effects in relieving disturbances of behavior.

MICHIGAN SCCIETY OF NEUROLOGY AND PSYCHIATRY

LEO H. BARTEMEIER, M.D., *President, in the Chair*

Regular Meeting, Sept. 28, 1944

Psychiatry and Demobilization. DR. GEORGE H. PRESTON, Baltimore.

If one thinks from a psychiatric point of view about what happens when armies are disbanded, it is obvious that the term "demobilization" fails to describe the process adequately. Men do not become immobile when they leave the army. They are supposed to begin living again. From a military point of view the army stops moving and is demobilized. From the civilian point of view men who were demobilized by the army must get going again, must be remobilized.

Remobilization in this sense has psychiatric implications. Healthy development is a continuous process,

† Dr. Ziegler died Jan. 8, 1945.

in which the solution of each day's problems rests on the accumulated traces of past experience. The measure of adequacy of mental health is the extent to which past experience provides the individual with skills and defenses suited to the demands of the culture in which he lives. If this continuous process is broken or if the step by step development is twisted so that one step does not prepare for the next, he may find himself confronted, at some point in his life, with a barrier he cannot reach over, avoid or charge through. Military training introduces two disturbing factors: interruption of the orderly day by day process by which suitable civilian experience is acquired, and the introduction of much experience totally unsuitable for civilian life. The time in the man's life at which interruption occurs is of vital importance. It is from this point of view that the problems created by military training and return to civilian life are important.

The problem before us today is the remobilizing of men whose orderly process of development has been interrupted. The stage of development which the man had reached at the time the interruption occurred is of importance. The problem rests more heavily on the younger men, who have not yet attained full adult independence and responsibility, and its seriousness probably varies in intensity as one moves from the agricultural through the mechanical trades groups toward the men in the white collar jobs and the professions. When men return to civil life, it is obvious that they will be thrown more or less suddenly into situations which they expect to find familiar but which, because of changes within themselves, will seem strange. The frustration which results from such unfamiliarity is well known to all psychiatrists. If that were the only factor with which psychiatry will have to deal, the problem would not be so complicated. Unfortunately, other elements enter the picture. Among these are resentment, which often exists in military service, and the effect of living in the closely knit units which are necessary to military routine.

In demobilization this country must deal with several million young men who have become adult without having had time to learn adult responsibility in a socializing situation, landing in a strange and frustrated situation, trained to belong to closely knit units and filled with the experience of destroying any one who does not belong. This is the problem which this country must face and to which the psychiatrist must be ready to make his contribution. If efforts are not successful in breaking down these close-knit, resentful, bewildered groups, it is obvious to any psychiatrist that the compromises and the give and take necessary for a democratic government will be almost unobtainable. It will require wise planning and prompt execution to prevent serious results. These are matters with which psychiatric organizations all over the country should be deeply concerned.

Book Reviews

Personal Mental Hygiene. By Dom Thomas Verner Moore, M.D. Price, $4. Pp. 331. New York: Grune & Stratton, Inc., 1944.

Psychiatrists returning from the military camps and war zones tell of a new source of referral of psychiatric cases—the chaplain. The psychiatrist who was accustomed to receive his clientele largely from exhausted families, bewildered employers and exasperated internists now becomes aware of a new orientation in reporting to or consulting with this new referring agency—the religious branch of the armed forces. Indeed, the mentally ill soldier, sailor or aviator is likely to turn for aid either to the post chaplain or the hospital psychiatrist or to both.

The appearance of Father Thomas V. Moore's "Personal Mental Hygiene" is therefore particularly welcome at this time. It is a book on the preventive aspect of psychiatry written by a man with a distinctly religious philosophy of life. The combination of priest and psychiatrist, while rare in this day and age, is by no means contradictory. The priest has long been functioning in a psychiatric capacity, and the office psychiatrist, consciously or unconsciously, assumes a pastoral role.

However, the combination is also not without its inherent difficulties. These could be summarized as the dangers of "colored judgment" and of "sitting in judgment." The author deals with both problems with variable degrees of success, but with much sincerity and ardor. He frankly asserts that he is devoted to his Roman Catholic Church and does not apologize for having chosen his axioms from its theology. The only thing that one has a right to expect in such a situation is the attitude expressed in a conciliatory letter from one chaplain to his colleague. "Let's stop quarreling," he writes, "it isn't good for the morale of our men. I have arrived at the conclusion that I am perfectly willing to let you serve the Lord in your way, as long as I serve Him in His way."

As for the attitude of sitting in judgment on the patient, instead of the noncondemning relationship of present day psychiatry, the author may be said to have achieved a large measure of success. The style of the book is in many places rather sermonic, but rarely "preachy." The scolding and the hortatory form makes room for the religious teacher's power of illustration. The book offers not only psychiatric expositions but a worth while cultural experience. The author chose the poet's insight into the dynamics of personality as a short cut to analytic understanding. Thus, Oliver Goldsmith is presented as a case of the "creative psychopathic personality," and there follow Rossetti, Swinburne, Francis Thompson and Joyce Kilmer as universal psychologic types.

The book treats of a great variety of subjects: religious scrupulosity, aggressiveness and depression, the rejected and the overprotected child, and the specter of divorce constantly threatening the integrity of the modern family. There is a very readable chapter on the "enjoyment" of prejudices in race hatred; and in the perennial problem of freedom or discipline in school, St. Anselm is shown to be a forerunner of Pestalozzi. However, there are three outstanding aspects of the book which lend it much distinctiveness, namely: (1) the interplay of intellect and emotion in life; (2) the author's attitude toward psychoanalysis, and (3) the positive values of religious sublimation.

The author takes up cudgels for a greater role in psychiatry of ideologies, principled goals and habits of thinking. These he feels (and he is by no means alone in his contention) have been sadly neglected in understanding or helping the neurotic and paranoid personalities. The author was brought up on St. Anselm and Thomas Aquinas and the other great representatives of scholasticism. He is enamoured of the intellectual life. However, he makes a distinction between the form of reasoning, of syllogism and logic, on the one hand, and the major premises, on the other. The reason that these attain to the dignity of axioms is because they have their roots in the bedrock of the emotional life. But then, again, strong emphasis is placed on the distinction between mere animal emotion, which is largely sensational, and the human emotions, which have their indissoluble intellectual connections.

His attitude toward psychoanalysis may be said to be ambivalent. He is at least on speaking terms with the "unconscious" (especially in dream interpretation) and uses a fair number of psychoanalytic terms and principles in explaining the causation of mental conflict. However, he reserves the right to explain in terms of his own philosophy the miracle of the transition from defense mechanisms to the heights of sublimation.

The most constructive aspect of the book is of course the delineation of the domain of religious psychotherapy. This type of therapy, the author asserts, is infinitely more than the retailing of the "milk of human kindness." It requires the exploration and mobilization of basic tendencies and concepts of the personality in meeting particular life situations. He rejects vehemently the conception of religion as an obsessional neurosis on a universal scale. Such an idea of religion he feels is not only therapeutically barren but philosophically inadequate. He insists with warm conviction that religious psychotherapy is indispensable in man's acceptance of his limited roles in society and the universe and the extension of his "time horizons of success" (to use a term of Schilder's), and therefore must become the basis of a psychology of goals and values differentiating mere pleasure from the totality of happiness.

How to Influence Yourself. By K. Morlan, Ph.D. Price, $2.50. Pp. 237. East Chatham, N. Y.: Berkshire Press, 1944.

Every so often a theatrical critic feels it necessary to discuss the question whether or not reviews would be better written by persons who are not specialists in their field, since the viewpoint of the person who sees play after play tends to become warped and the value of his opinion to the ordinary theatergoer thereby diminished. A similar question arises here, when a psychiatrist has to review a book which is written primarily for laymen. Would not a person for whom this book is intended be in a better position to say whether it could help him? A book of this sort is bound to appear naive to the specialist, and the latter

could quite easily look down his nose at it. There is, however, some reason for the psychiatrist to venture an opinion, since he is frequently asked by patients what they could read that might clarify things for them. It is with this idea in mind that I find some justification for my review.

The author is the dean of men and teaches mental hygiene at the Polytechnic Institute of Puerto Rico. Throughout, one has the impression of a humane person, who has seen and heard a great deal and who is imparting the results of his observations in the form of "common sense" rules of living. The tendency of people writing books of this sort is to talk down to the reader, telling him dogmatically that this is what he should do and this is what he should not do to attain full adjustment. Although the author slips into this error rather frequently, there is still enough open-mindedness not to make the book as obnoxious as such books can sometimes be. Throughout, the author refers to interesting case histories and illustrates his material with numerous examples. Many of the current psychiatric viewpoints are represented rather accurately in simple, everyday language, so that in a general way the ordinary layman is oriented correctly. Whether this will help him particularly is another question. Perhaps a person suffering from superficial personality difficulties will find something in this book to help him, but I doubt whether the patient with a full blown neurosis will get anything out of it. It is known that the mere intellectual awareness and knowledge of a problem does not necessarily lead to cure. The value of this book lies mostly in the fact that the reader's attention is called to the possibility that he can do something about his problem even if it is not as simple as would appear to be suggested by the author.

Poet Physicians: An Anthology of Medical Poetry Written by Physicians. Compiled by Mary Lou McDonough. Price, $5. Pp. xiii, plus 210, with index and bibliography. Springfield, Ill.: Charles C Thomas, Publisher, 1945.

Most medical poetry is doggerel written for amusement and recreation by busy doctors. However, once in a while an inspired physician produces a poem that can rank with the best of the lyric poetry of his generation. The medical man will view these efforts with greater interest than he will those of men who have had medical training but who are known chiefly as poets, such as Keats and Goldsmith. McDonough has selected the best from the large number of poems available and has included brief sketches of the lives of both living and dead, from many countries.

Old favorites, like "The Chambered Nautilus" and "In Flanders Fields," rub elbows with poems by doctors about doctors. Actually, doctors in the main do not make very good poets. There is a fatalistic, elegiac character about their verse. Death is a natural preoccupation, but many of the poems represent a looking back on life with the philosophy but without the freshness of long acquaintance. Medical poets are old, or at least they sing in the words of old men. Curiously, no woman's name is found in the bibliography of over 400 names. It is difficult to compare living poet-physicians, like Tucker and Moore, with those of a bygone age, like Fracastoro, and even the Elizabethan poet-physicians. There were giants in those days, but they spoke in different idiom. Somehow, the power of verse to evoke images is used to better effect by some of our contemporaries than by those who have gone before. The compiler has spared the reader from *vers libre*, from long poems and from doggerel, for which she is to be thanked. However, in the lyric poetry presented there is almost too great preoccupation with death. There is a solemnity about many of the poems that probably belies the vigorous character of their authors. Humor is often toned with the macaber. The book is elegantly printed on paper that will not reflect the light from the bedside lamp. Many physicians, poets or not, will rejoice in this delightful collection of the inspirations of their colleagues, living and dead. And some may be led to postpone no longer their own efforts to put on paper the results of their own profound thinking.

News and Comment

CANCELLATION OF ANNUAL MEETING OF AMERICAN NEUROLOGICAL ASSOCIATION

The meeting of the American Neurological Association which was scheduled to be held this year has been canceled because of failure to receive permission for the holding of the meeting.

CORRECTION

In the article by Dr. M. J. Madonick and Dr. Ignaz W. Oljenick entitled "Displacement of the Pineal Gland with Extradural Hemorrhage," in the April issue (ARCH. NEUROL. & PSYCHIAT. **53**:311, 1945), the second sentence in the first paragraph, second column, should read:

"The pineal gland was displaced 1 cm. to the right of the midline, 1 cm. posteriorly and 0.5 cm. downward (figure, *B*), according to the method of Vastine and Kinney."